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EOSINOPHIL CELLS IN THE BLOOD OF NORMAL AND OF ASTHMATIC CHILDREN *

KAJ H. BAAGØE

Formerly Assistant Physician to the Children's Department, Rigshospitalet

COPENHAGEN, DENMARK

NORMAL CHILDREN

While it is commonly agreed that the number of eosinophil cells in adults is normally about from 2 to 4 per cent, the greatest uncertainty prevails with regard to children. Most authors state that the number of eosinophil cells is larger in children than it is in adults (Zappert,[1] Gundobin,[2] Carstanjen,[3] Rabinowitsch,[4] Schmidt [5] and others). A few writers (Rosenstern,[6] Putzig [7] and others) state, however, that the number of eosinophils is the same in healthy children as it is in adults; they consider the high values found by other writers due to the fact that the children examined were not healthy. The question with which I am concerned here, however, is not so much the reason for the high values, as it is the nature of the blood picture in apparently healthy or normal children.

In order to elucidate this matter, I shall present in this paper the material on which my interpretation of the blood picture in normal children rests. For this purpose, I have selected the three largest series of investigations published during recent years, which have been made by Rabinowitsch (Bern), Carstanjen (Innsbruck) and Schmidt (Copenhagen). These authors have examined 60, 112 and 128 children, respectively, or a total of 300, aged from 3 to 14 years.

REVIEW OF THE LITERATURE

Carstanjen examined children who either stayed in the hospital or consulted the polyclinic for "external diseases," and he said that with

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1. Zappert, J.: Ztschr. f. klin. Med. **23**:227, 1893.
2. Gundobin, N.: Besonderheiten des Kindesalters, Berlin, 1912.
3. Carstanjen, M.: Jahrb. f. Kinderh. **2**:215, 333 and 684, 1900.
4. Rabinowitsch, D.: Untersuchungen über die Leucocyten gesunder Kinder, Dissertation, Stuttgart, 1912.
5. Schmidt, V.: Hæmatologiske Studier (Disputats), Copenhagen, 1924.
6. Rosenstern, J.: Jahrb. f. Kinderh. **69**:631, 1909.
7. Putzig, H.: Ztschr. f. Kinderh. **9**:429, 1913.

regard to the blood picture the children may be considered "healthy." The majority of the children belonged to the poorer classes. Two thousand cells were counted in each count.

Rabinowitsch examined healthy children who accompanied the patients to the polyclinic; he counted 300 cells.

Schmidt examined children who came with the patients to the polyclinic, and children from nurseries; he counted 400 cells.

Schmidt examined forty-six normal children and eighty-two children who had adenoids. He found a slightly higher average number of eosinophils in the children with adenoids (4.35 per cent) than in normal

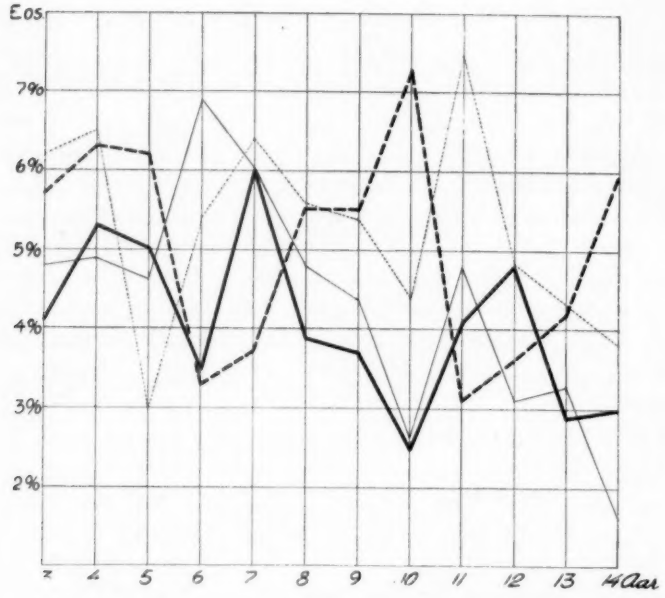

Chart 1.—Curves showing eosinophils in normal children in different age groups. The darker broken line indicates the results of Carstanjen; the lighter broken line, those of Rabinowitsch; the darker continuous line, those of Schmidt for normal children and the lighter continuous line, those of Schmidt for children with adenoids.

children (4.06 per cent). A closer study of his values shows, however, that this slight difference is due not to the fact that the number of eosinophils is higher in the children with adenoids than in the normal children, but to the fact that a small number of the children with adenoids had a relatively high number of eosinophils (from 9 to 12 per cent). As this number is well within the normal limits, I have included his two groups under the designation "normal" children in the following investigations.

When the material of the three authors is studied, it is seen that the number of eosinophils present in the blood of normal children varies greatly. Thus, Carstanjen has observed from 0 to 16 per cent of these cells; and Rabinowitsch and Schmidt, from 0 to 12 per cent.

It might be thought that the cause of the great variations in the number of eosinophils was to be found in the varying ages of the children, as has been suggested by some authors. This is hardly the case. If curves are drawn showing the variations in the number of eosinophils according to the age of the children, as stated by the three authors (chart 1), it will be seen that these curves fluctuate considerably, each one being different from the others. If taken collectively, on the other hand, they show a decrease in the number of eosinophils with increasing

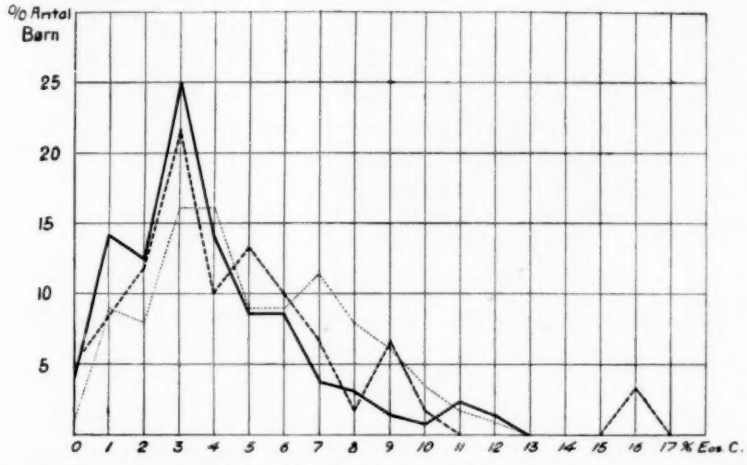

Chart 2.—Curves showing eosinophils in the total number of normal children. The darker broken line indicates the results of Carstanjen; the lighter broken line, those of Rabinowitsch and the continuous line, those of Schmidt.

age, as might be expected, since the number of eosinophils in adults is approximately from 2 to 4 per cent.

A more satisfactory agreement between the investigations made by these three observers is obtained by distributing the figures in the curves according to the percentage of eosinophils in the blood, as shown in chart 2. From this curve it will be seen that all three observers have in their series a few children with a high number of eosinophils, and also that the number that all three investigators found most frequently was 3 (-4) per cent.

Thus, if these three curves are made into a joint curve, a curve showing the number of eosinophils in "normal" children between the ages of 3 and 14 years is obtained, and in the following investigations this curve will be used as the "normal" curve.

For the purpose of comparing the "normal" curve of children with that of adults, the figures found by Zappert and Carstanjen in seventy-three "normal" persons more than 15 years of age are shown in table 1.

The figures in table 1 show that while the normal curve for children has its maximum at 3 per cent, a corresponding curve for adults has its maximum at 2 per cent. According to this, there seems to be no doubt that the blood of children "normally" contains a greater number of eosinophils than that of adults.

In order to demonstrate that a disease in children is accompanied by eosinophilia, it is necessary that a curve indicating the distribution

TABLE 1.—*Data of Zappert and Carstanjen for Seventy-Three Normal Persons*

Eosinophil Cells, Percentage	Number of Normal Adults
0	2
1	18
2	28
3	11
4	5
5	1
6	2
7	2
8	1
9	1
10	1
11	1

TABLE 2.—*Number of Normal Children with Less Than and Those with More Than 5 Per Cent Eosinophil Cells*

	< 5 per Cent Eosinophil Cells	> 5 per Cent Eosinophil Cells
Rabinowitsch	56	56
Carstanjen	34	26
Schmidt	89	39
Total	179	121

of the percentage contents of eosinophils for the children concerned should be found displaced to the right in relation to the normal curve, so that the maximum of the curve is to the right of 3 per cent.

In deciding whether a disease in children is accompanied by eosinophilia, another and quicker method may be used. Examination of the material of the three investigators already mentioned shows how many normal children have less than 5 per cent of eosinophils and how many have more than 5 per cent; the results are given in table 2.

Rabinowitsch's material comprises the same number of children with less than 5 per cent of eosinophils as those with more than this percentage, while the majority of the children examined by Carstanjen and, more especially, those examined by Schmidt, were below 5 per cent.

Thus, according to the investigations made by these three observers, the quotient:

$$\frac{\text{number of children with} > 5\% \text{ eosinophil cells}}{\text{number of children with} < 5\% \text{ eosinophil cells}}$$

is either equal to or less than 1.

If, therefore, this quotient is larger than 1 in a group of children, aged from 3 to 14 years, who are suffering from the same disease, it may be taken to indicate that the disease is accompanied by eosinophilia.

It will be seen from what has been said that in order to determine whether a disease in children is accompanied by eosinophilia, it is always necessary to examine a series of patients. If the question is asked, What importance may be attached to ascertaining the eosinophil content of the blood of a patient? it can be answered only by saying that when more than 10 per cent of eosinophils is present, it practically always indicates that the patient has eosinophilia, while a content of from 5 to 10 per cent is not a certain indication in this respect.

As will be apparent from what has been said, a content of from 5 to 10 per cent may well indicate a pathologic increase in the number of eosinophils, examples of which will be given later, and a content of from 5 to 10 per cent should accordingly be considered a "possibly" pathologic symptom.

ASTHMATIC CHILDREN

Differential counts were made in 124 asthmatic persons (ninety-two children and thirty-two adults), once or several times during the period in which they have been under observation. In all, 685 double counts were made. As a rule, the blood for the counts was taken during the afternoon, between 5 and 7, most frequently immediately before the evening meal.

The blood was spread over the slide in a layer of such thickness that the blood corpuscles were still partly arranged in chains. This insures an even distribution of the white cells over the whole film, and prevents the "dragging along" of the large cells (polymorphonuclear leukocytes and monocytes) by the concave fluid surface, which, as has been proved by Meulengracht, may happen when thinly smeared films are used.

The films were fixed in methyl alcohol and stained in May-Grünwald's stain.

Before discussing the number of eosinophils in the total number of patients, I will mention a few serial counts made in four children with asthma.

CASE 1.—Inga, aged 11 years, had been admitted to the hospital three times. On each occasion she had had many attacks of asthma immediately prior to admission and occasionally also during the first few days in the hospital, but later

during her stay she had been either completely or almost free from attacks. During her first and second stay, only a few blood counts were made, ten and twelve counts, respectively (chart 3). During her third stay, which extended over four months, thirty-six counts were made (chart 4).

It will be seen from the curves that the number of eosinophils in the blood fluctuated, although the number was always greatest during the first few days or weeks after the patient was admitted to the hospital

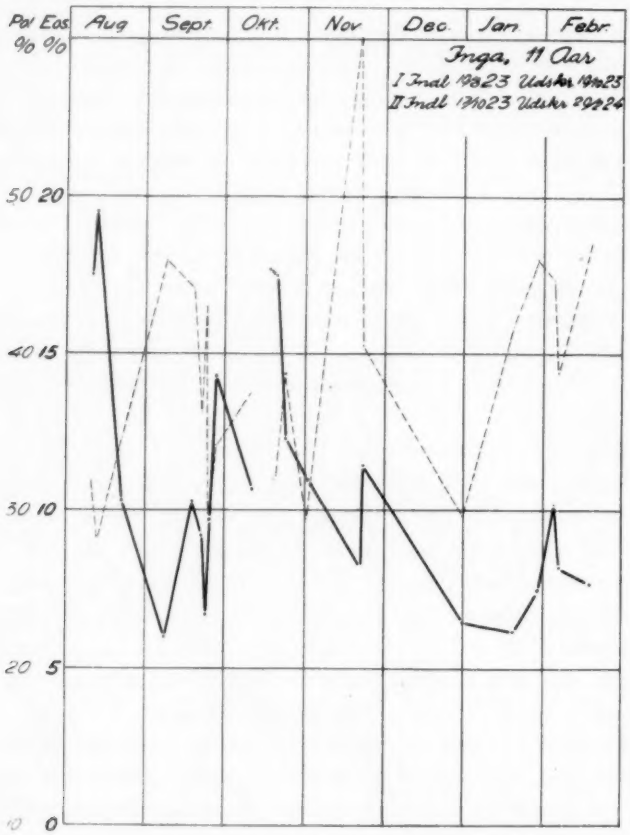

Chart 3.—Results of ten and twelve blood counts in patient in case 1 during her first and second stay in the hospital. The continuous line indicates the eosinophils; the broken line, the polymorphonuclear leukocytes.

(from 15 to 19 per cent) and showed a decline during the patient's stay in the hospital. During her last stay, she was treated with goose feather vaccine, and this may possibly have exerted some influence on the shape of the curve.

CASE 2.—Carl, a boy, aged 11 years, had thirty-four differential counts made during his stay in the hospital, which extended over two and one-half months

(chart 5). He had had many attacks immediately before being admitted, but he did not have any attacks while he was in the hospital. On the first two days after admission, there was 9 per cent of eosinophil cells, while during the rest of his stay, the number fluctuated around 5 per cent.

As the boy gave a positive reaction to skin tests with lobster, he was given 250 Gm. of lobster to eat. This did not produce any clinical symptoms or any changes in the blood picture.

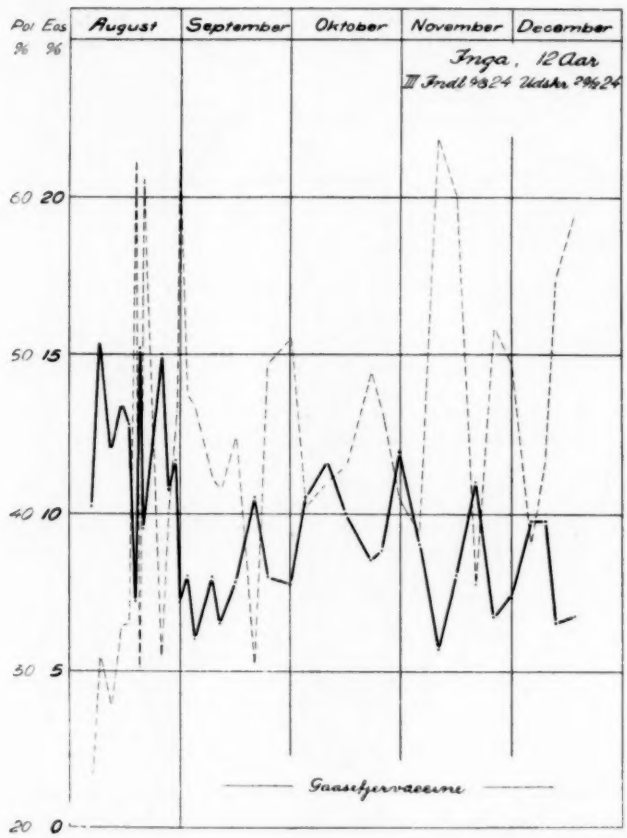

Chart 4.—Results of thirty-six blood counts in patient in case 1 during her third stay in the hospital. The continuous line indicates the eosinophils; the broken line, the polymorphonuclear leukocytes.

CASE 3.—Knud, a boy, aged 13 years, had not had any attacks during the two months prior to admission, and he was free from attacks during his whole stay in the hospital, which lasted for four months. Sixty-one blood counts were made (chart 6). When admitted to the hospital, he had 10 per cent of eosinophils, but this number quickly dropped to about 5 per cent.

As the boy showed a positive cutaneous reaction to lobster, for experimental purposes, he was given 250 Gm. of lobster three weeks after admission. He ate the lobster with a good appetite and did not develop either asthmatic attacks or

urticaria. The only result possibly attributable to the lobster was that a herpetic lesion the size of a pea broke out on his lip on the following day. The number of eosinophils, on the other hand, was considerably increased; from March 15 to April 3, about 10 per cent of eosinophils was found; this number afterward dropped to below 5 per cent.

When the number of eosinophils had remained constantly at this level for about a fortnight, the patient was again given 250 Gm. of lobster. This time also he developed a small outbreak of herpes on the lip on the following day. Four days later, the number of eosinophils rose to 10 per cent, at which level they remained from May 4 to May 19; they then showed a steady decline.

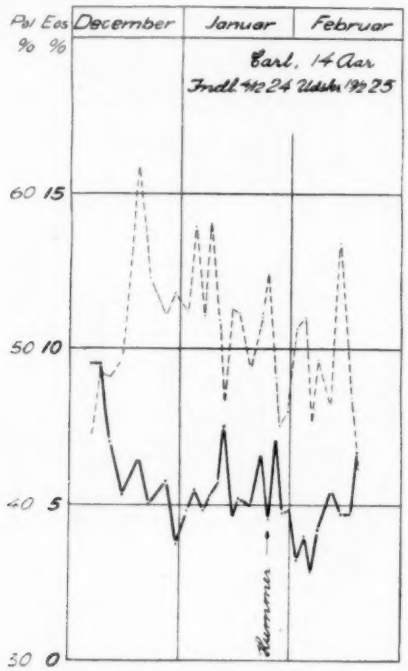

Chart 5.—Results of thirty-four blood counts in patient in case 2. The continuous line indicates the eosinophils; the broken line, the polymorphonuclear leukocytes.

Thus it will be seen that on both occasions the eating of lobster was followed by a rise in the number of eosinophils; in both instances the high figure persisted for about a month. This increase in the number of eosinophils may possibly be interpreted as a reaction on the part of the organism caused by the child's hypersensitiveness to lobster, as was indicated by his positive cutaneous reaction to this food; but the facts that other causes of the eosinophilia may exist and that the eosinophilia might have appeared even if the boy had not eaten lobster cannot be excluded.

Whatever may be the reason for the increase, this case shows that marked eosinophilia may appear in an asthmatic person without being immediately preceded by asthmatic attacks.

CASE 4.—Magnus, a boy, aged 10 years, had had frequent attacks until three weeks before admission; during his stay in the hospital, which lasted for five months, he did not have any attacks. In all, fifty-six blood counts were made

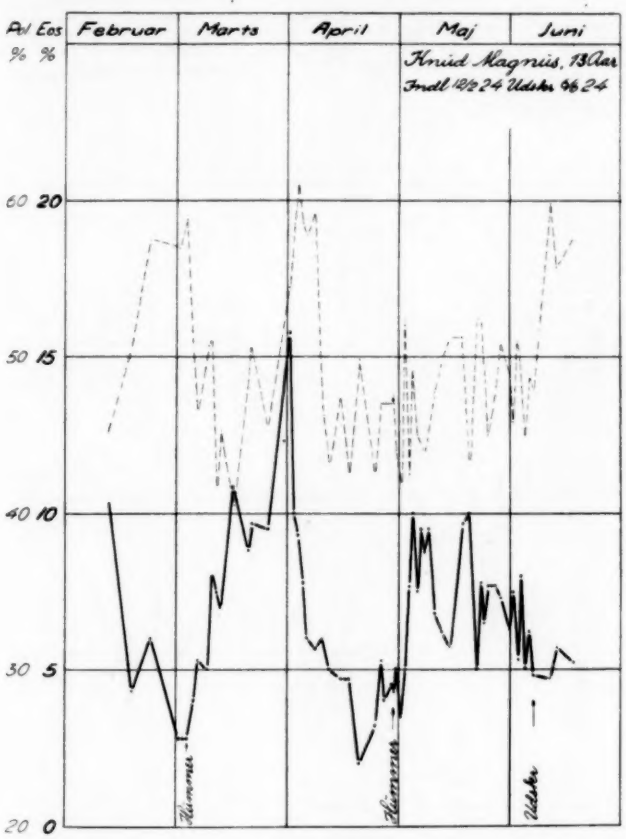

Chart 6.—Results of sixty-one blood counts in patient in case 3. The continuous line indicates the eosinophils; the broken line, the polymorphonuclear leukocytes.

(chart 7). On admission, the patient showed rather marked eosinophilia (up to 15 per cent), but during his stay, the number of eosinophils decreased. The curve shows considerable fluctuation during the first month or so. The strong decline, which occurred a few days after admission, can possibly be explained by the rise in temperature to 40 C. (104 F.) as, according to Zappert, a rise in temperature is capable of producing a decrease in the number of eosinophils. During the rest of his stay in the hospital, the patient's temperature was normal.

The curves for patients 1 and 2 (charts 3, 4 and 5) confirm the statement made by von Noorden [8] that the eosinophilia is highest following a period during which there are many attacks, but neither in these patients nor in others have I observed the disappearance of the eosinophilia during the attack which Heinecke and Deutschmann [9] and Salecker [10] said occurs.

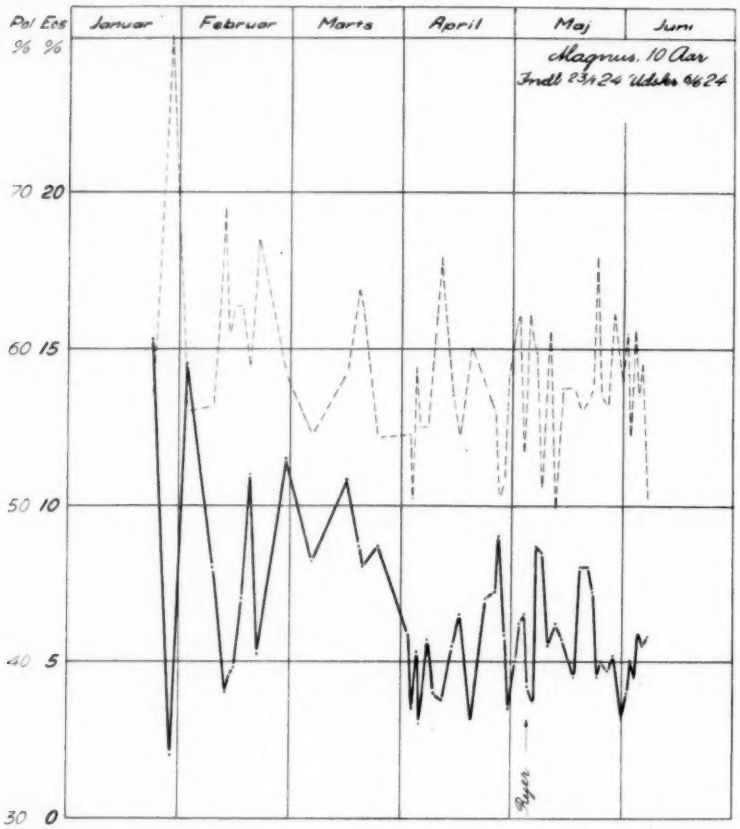

Chart 7.—Results of fifty-six blood counts in patient in case 4. The continuous line indicates the eosinophils; the broken line, the polymorphonuclear leukocytes.

In case 1, the average quantity of eosinophils in the blood was 10.1 per cent; during five attacks, it was 9.2, 18, 8.2 and 4.7 per cent, respectively. In another asthmatic child in whose blood the average

8. Von Noorden, C.: Ztschr. f. klin. Med. **20**:98, 1892.

9. Heinecke, A., and Deutschmann, F.: München. med. Wchnschr. **53**:797, 1906.

10. Salecker, P.: München. med. Wchnschr. **54**:358, 1907.

eosinophil content was 7.2 per cent, the content during ten attacks changed to 8.1, 6, 5, 5.7, 4.5, 10.5, 6.7, 6.2, 8.7 and 5.2 per cent, respectively.

From these serial counts it appears further that the eosinophilia following a period during which the patient has many attacks either decreases or disappears completely at a subsequent period during which he does not have any attacks (patients 1 and 2), and that eosinophilia

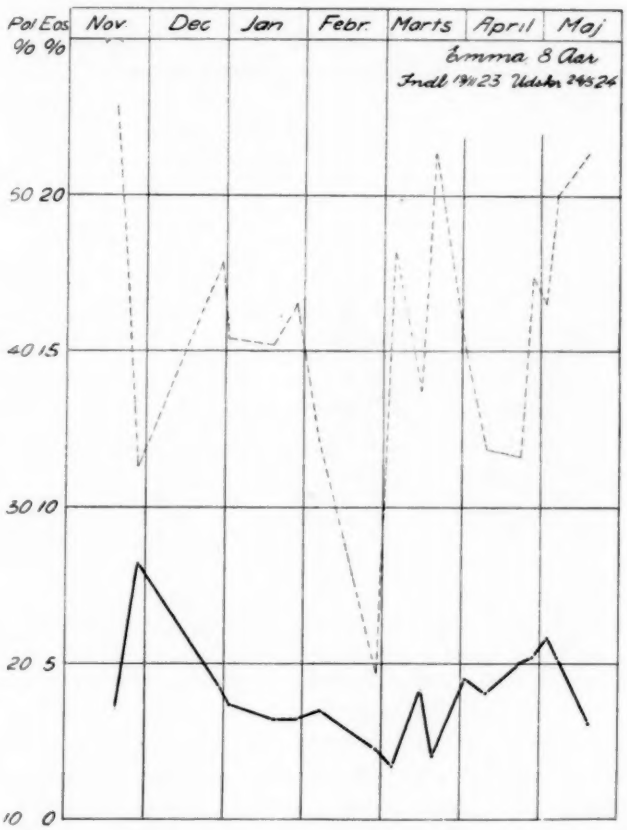

Chart 8.—Results of eighteen blood counts in patient in case 5. The continuous line indicates the eosinophils; the broken line, the polymorphonuclear leukocytes.

may also appear when he has not had attacks immediately before the condition develops (patients 3 and 4).

The last case that I shall mention is that of a patient who, in spite of frequent attacks, did not develop a perceptible eosinophilia.

CASE 5.—Emma, a girl, aged 8, had had asthmatic attacks every night during the last month prior to admission to the hospital, where she stayed for six months. During the first four months she had only occasional attacks with intervals of

several weeks, but during the last two months she had from one to two (even four) attacks every day. Eighteen blood counts were made during her stay in the hospital (chart 8). As will be seen from the curve, there was scarcely any eosinophilia; it is true that a slight decline may be seen during the first few months, as well as a slight increase during the last months, but with a single exception, all the figures were below 5 per cent. The average was 4 per cent.

This case shows that occasionally a patient may have many attacks without developing a distinct eosinophilia.

CONDITIONS IN ASTHMATIC PERSONS

The patients studied are divided into three groups: (1) fifty-two children treated in the hospital, (2) forty ambulant children and (3) thirty ambulant adult patients (above the age of 16).

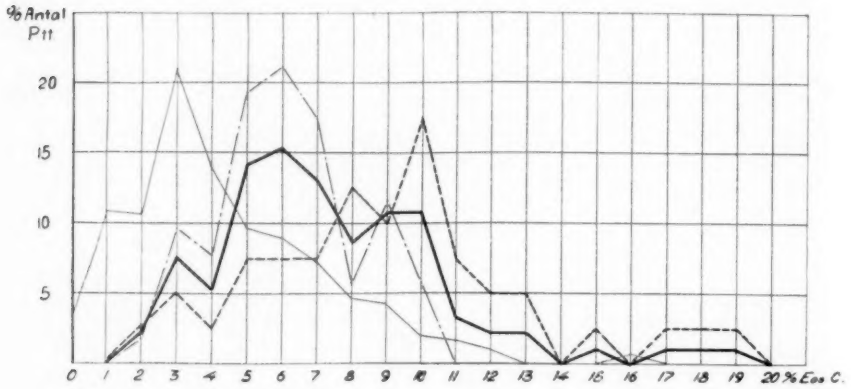

Chart 9.—Curves showing eosinophils (average number) in ninety-two asthmatic children. The darker continuous line indicates the total number of asthmatic children; the dot and dash line, the children in the hospital; the broken line, the ambulant children, and the lighter continuous line, the normal curve.

The average numbers of eosinophils in these three groups were: children treated in the hospital, 6.6 per cent; ambulant children, 9.5 per cent, and adults, 7.3 per cent.

The first point to be determined during an examination is whether eosinophilia is present. I have used the method mentioned and have drawn a curve according to the percentage content of eosinophils in the blood; I then compared this curve with the "normal" curve. The two curves are not exactly homologous, as the normal curve is based on individual counts, and the percentage has been calculated in relation to the absolute number of leukocytes; while the curve for asthmatic persons, most of whom were children, is based on the average of several counts and the relative number of eosinophils. The percentage of children examined in different age groups is nearly the same, namely,

150 "normal" children, aged from 3 to 8; 150 children, aged from 9 to 14; 43 asthmatic children, aged from 1 to 8, and 49, aged from 9 to 15.

From chart 9 it may be seen that the curve for all of the ninety-two children shows two peaks, one at from 5 to 7 per cent and a lower one at from 9 to 10 per cent. That the curve shows two peaks is not accidental, but is due to the fact that the material is heterogeneous, being made up of two different groups of patients: children treated in the hospital and ambulant children. If the curve is separated into two curves, each corresponding to its group of patients, it will be seen that the curve for the children in the hospital has its peak at from 5 to 7 per cent, while the curve for ambulant children has its peak at 10 per cent.

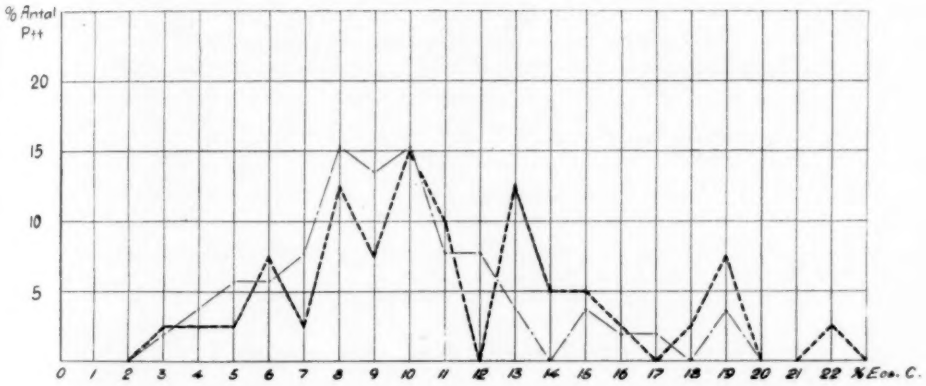

Chart 10.—Curves showing eosinophils (maximal number) in ninety-two asthmatic children. The dot and dash line indicates the curve for the children in the hospital and the broken line, that for the ambulant children.

In comparing these two curves with the "normal" curve, it is seen that both curves are displaced to the right in relation to that curve. This proves that a pathologic increase in the number of eosinophils is present in the majority of asthmatic persons in both groups.

The different courses taken by the two curves for hospital children and ambulant children should presumably be explained by the fact, previously mentioned, that the content of eosinophils in the blood is higher, as a rule, after many attacks and lowest in periods during which there were no attacks.

The children treated in the hospital practically never had any attacks while they were in the hospital. For this reason, a series of blood counts made for the hospital patients showed comparatively low average numbers of eosinophils, even if marked eosinophilia had been present during the first few days after admission. The reverse was

the case with the outpatients. As a rule, these patients appeared for examination immediately after a series of attacks of asthma; accordingly, their blood contained a larger number of eosinophils.

If, on the other hand, the maximum numbers in the two groups of patients are compared, it is found that almost no difference exists. Chart 10 shows that the two curves nearly coincide.

It has not been determined whether the age of the patients has played an essential rôle with regard to the degree of eosinophilia.

The average numbers of eosinophils are 8.3 per cent in the age group from 1 to 5 years, and 7.3 per cent, from 5 to 10 years 7.9 per cent from 10 to 15 years (by hospital patients, 6.3, 6.5 and 6.7, respectively, and for outpatients, 11.8, 8.7 and 8.8 per cent, respectively).

TABLE 3.—*Number of Patients in Different Age Groups with Less Than and Those with More Than 10 Per Cent of Eosinophils*

	1 to 5 Years	5 to 10 Years	10 to 15 Years	15 to 20 Years	20 to 40 Years	Above 40 Years
< 10 per cent eosinophil cells...	9	18	14	6	10	8
> 10 per cent eosinophil cells...	8	23	16	6	5	1

TABLE 4.—*Proportion of Eosinophil Cells in Blood Counts Made at Intervals*

	Eosinophil Cells						
Blood Count	0% 1% 2%	3% 4%	5% 6%	7% 8%	9% 10%	>11%	Average per Cent
Shortly after admission Number of patients.....	2	5	4	7	5	5	7.7
After no attacks for at least one month Number of patients.....	3	3	12	7	2	1	6.1

The data in table 3 show that eosinophilia of more than 10 per cent was found to be equally frequent in children of all age groups. In adults, the frequency with which a high degree of eosinophilia was present seemed to become less with increasing age.

On the strength of these examinations of average and maximum numbers, the age of the child does not seem to play an essential part with regard to the number of eosinophils.

It was seen from the serial counts that the eosinophilia subsided or disappeared during the patient's stay in the hospital. The data in table 4 serve to show whether asthmatic persons have had the number of eosinophils reduced to normal after an extended stay in the hospital.

The results given in table 4 were obtained in twenty-eight children in the hospital in whom blood counts were made shortly after admission and shortly before discharge and also after the patients had not had any attacks for at least one month during their stay in the hospital.

The figures show that after a period of at least one month during which the patient did not have any attacks, the average number of eosinophils was a little lower than that on admission. The question is, Had the number of eosinophils become normal when the patient was discharged?

It is true that the number of eosinophils found on various counts at the time of the patient's discharge was normal, but the highest point of this curve is at 5 or 6 per cent, which means that it is displaced to the right in relation to the "normal" curve, which has its peak at 3 per cent. It is to be presumed, therefore, that although these children had been free from attacks for at least one month, there was still a pathologic increase in the number of eosinophils.

SUMMARY

1. In normal children, aged from 3 to 14 years, the number of eosinophils varies considerably, as different observers have found values from 0 to 12 per cent; the percentage of eosinophils most frequently found, however, was approximately 3 per cent. The age does not seem to have any particular effect on the degree of eosinophilia in normal children, as merely a slight decline was observed with increasing age.

2. Differential counts were made in 124 asthmatic persons: ninety-two children and thirty-two adults. A number of serial counts showed the following:

(*a*) The number of eosinophils may be increased after a series of attacks, this increase either subsiding or totally disappearing during a subsequent period during which there are no attacks.

(*b*) The number of eosinophils may suddenly be increased, although there has not been an asthmatic attack immediately before this occurs.

(*c*) The number of eosinophils may occasionally be nearly normal during periods in which the patient has many attacks.

3. The average number of eosinophils was higher in ambulant children than in children treated in the hospital; this probably has some connection with the fact that the children who were treated in the hospital were free from attacks during their stay in the hospital.

4. The eosinophilia did not disappear during the asthmatic attack.

5. The age of the children did not seem to have any bearing on the degree of eosinophilia.

6. During the patient's stay in the hospital, the number of eosinophils decreased, but was still pathologically increased after a period of one month during which the patient did not have attacks of asthma.

INTRADERMAL VACCINATION *

JOHN A. TOOMEY, M.D.
AND
ROBERT B. HAUVER, M.D.
CLEVELAND

Many physicians have reported high percentages of successful vaccinations by the intradermal method (Starkey,[1] Berney,[2] Twyman,[3] Wright [4] and Simko [5]). Leiner and Kundrawitz [6] vaccinated fifty children with 0.1 cc. of a 1 : 100 dilution of vaccine and obtained positive and feverless reactions in thirty-nine, no reactions in five and atypical reactions in six. Singer [7] also claims that fever associated with intradermal vaccination is rare or of short duration, the reactions milder and the resultant scars less definite. Many authors (Kovacs,[8] Frankenstein,[9] Gettinger [10] and Hoffman [11]) believe that there is a decrease in secondary infections. Three hundred and twenty-one of Twyman's 397 patients, or 80.9 per cent, had positive reactions. Wright vaccinated intradermally 227 patients who previously had been vaccinated unsuccessfully as often as from two to eight times, with 160 successful vaccinations (70.4 per cent). These patients were vaccinated concurrently with the same virus and strength of dilution by the incision method with only 8.3 per cent

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* From the Department of Pediatrics, Western Reserve University, and the Division of Contagious Diseases, Cleveland City Hospital, Cleveland.

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11. Hoffman, W.: Intradermal Vaccination, Schweiz. med. Wchnschr. **51**:79 (Aug. 25) 1921; abstr. J. A. M. A. **77**:1212, 1921.

successful vaccinations. Sixty-seven of the areas intradermally vaccinated did not react; all except four, however, showed an immunity or "vaccinated" reaction, while of the 208 negative areas, few showed the immunity reaction (exact numbers not mentioned). Wright kept his vaccine in a glycerin-phenol-water solution (49-1-50), and to illustrate that the reaction was not due to this preservative, he vaccinated several persons with this solution, with negative results.

METHOD AND MATERIAL

All patients admitted to the contagious division of the Cleveland City Hospital (from July, 1922, to August, 1927) irrespective of histories of previous vaccinations, as well as all the new personnel, including nurses, physicians, attendants, porters and maids (approximately 9,000 in all) were vaccinated intradermally. In these groupings, there were 2,852 primaries (persons not previously vaccinated) who were followed up until the wound healed. About 287 other primaries were excluded from the report, as they left the hospital too soon for accurate observations. In addition, 180 primaries were vaccinated in a local orphan asylum.

The first few patients were given injections of a 1:100 dilution of vaccine; a very small scar was the final result. To increase its size, subsequent vaccine material was diluted only one to four +, physiologic sodium chloride solution being the diluent in all instances. The bulk vaccine [12] was used up rapidly, but the same rough proportion was kept by diluting the contents of a stock capillary vaccine tube with 3 drops of saline. One cubic centimeter of this 1 to 4 dilution from bulk or capillary vaccine was injected. A tuberculin syringe with a 27 gauge needle was used for the injections. When two methods of vaccinations were tried on the same person, they were always performed at the same time and with the same percentage strength dilution of vaccine virus. All routine vaccinations were performed by the residents or interns, but all readings and vaccinations for comparative purposes, for testing potency and other factors were done by us.

THE LESION

A typical positive reaction was a maculated lesion which developed from three to six days after vaccination; it pustulated in from five to twelve days, a scab formed in from eight to eighteen days, and the wound healed in from fourteen to twenty-nine days.

A reaction was considered negative if local evidence had not appeared by the seventh day. There were many atypical reactions or pseudo reactions, in most of which a hard glassy papule was produced from three to six days after vaccination; later a scab formed in from ten to twenty days. In some cases, especially in children, deeper vaccination possibly occurred with technical errors of injection, so that there would be a local, hard, indurated, indolent, deep-seated papule as early as the sixth day, while in other patients, this lesion would be associated with all the signs of an erysipelatoid inflammation. When this deep-seated lesion was let

12. Received from and through the courtesy of the Lederle Company.

alone, it finally ruptured and healed, leaving a minute scar at the point of rupture; there was little dimpling, as the remainder of the lesion was absorbed. In other instances, this deep lesion did not rupture, but continued hard and indurated; in about ten or twelve days, a raised pustule or hard glassy blister would appear, and a scab formed in from twelve to thirty days. Complete healing required a longer time in these cases, complete absorption occurring in from three to four weeks.

RESULTS

Of the 2,852 hospital primaries, twenty-three died before vaccination could have become effective and are not included in our computation by percentage; 2,506 of the remainder, or 88.5 per cent, had positive reactions. One hundred and seventy-nine of the 180 children in the orphanage (99 per cent) were vaccinated successfully.

Three hundred and twenty-three of the patients had negative or atypical reactions. Of the total 323 negative reactions, 101, or 31.2 per cent, occurred in patients over 2 years of age, while 221, or 68.4 per cent, occurred in patients under 2 years of age. There were 162 infants under 2 years of age among the 2,506 who had positive reactions, and the total number in the group of that age, infants with negative and positive reactions, numbered 383; of these, only 42.2 per cent gave positive reactions, while 221 or 57.7 per cent gave negative reactions. If only the patients over 2 years of age were considered and the twenty-three deaths ignored that occurred before vaccination could be effective, there would be 2,446, of whom 2,345, or 95.8 per cent, had positive reactions. In the entire group of 324 negative or atypical vaccinations, there were only forty-three clear-cut negative reactions (these subjects are termed for convenience, the first group) while there were 281 pseudo or atypical reactions (these subjects are termed for convenience, the second group). Revaccination in these two groups gave forty-two persons with negative reactions among those who previously gave clear-cut negative reactions, with one positive reaction. Subsequent vaccination did not change the reading. Among the persons with pseudo reactions, 263 of the 281 showed reactions of immunity within twenty-four hours after the second vaccination, and the general conclusion that pseudo reactions are positive reactions is not improbable. If the pseudo and positive reactions are considered and included as successful vaccinations, then the total number of hospital "positives" is 263 more than the original figure, making a total of 2,769 positive and sixty negative reactions, an average of over 97.8 per cent.

In another group, 150 primaries of over 2 years of age were vaccinated and compared with 150 primaries under 2 years. In the former group, 147 (98 per cent) were positive and three were negative, and in the latter, group 105 (70 per cent) were positive and forty-five negative.

Here, again, there were atypical reactions which probably could be termed positive. In the next experiment, 150 primaries over 2 years of age were vaccinated at the same time, once by the intradermal and again by the scratch method. There were 145 (96.6 per cent) positive reactions and five negative with the former method and seventy-two (48 per cent) positive and seventy-eight negative with the latter method.

In another experiment, eighty-two persons, physicians and nurses, who had previously been vaccinated unsuccessfully, each at least six

TABLE 1.—*Reactions to Weak Vaccines*

	Vaccine	Series	Number	Positive	Negative	Percentage
1	2 months before date of expiration	1	19	1	18	5
	2½ months before date of expiration	2	100	14	86	14
2	4 months before date of expiration	1	6	0	6	0
	4 months before date of expiration	2	42	2	40	4+
3	5½ months before date of expiration	1	12	5	7	41
	5 months before date of expiration (approximately)	2	37	21	16	56.7+
	Total		216	43	173	

TABLE 2.—*Paul's Test: Reactions to Weak Vaccines*

	Vaccine 1:1,000		Potent Virus	
	Vaccine Tested	Paul Test Right Eye	Control Vaccine (Potent)	Paul Test Left Eye
1	1:1,000	(—)	1:1,000	(+)
	1:500	(—)	1:500	(++++)
	1:100	(—)	1:100	++++ generalized keratitis
	1:25	(+)	1:25	++++ generalized keratitis
2	1:1,000	(—)	1:1,000	(+)
	1:100	(+?)	1:100	(++++)
	1:100	....	1:100	(++++)
	1:25	(—)	1:25	++++ keratitis
3	1:1,000	(—)	1:1,000	(+)
	1:100	(+)	1:100	(++++)

times, were vaccinated intradermally, which resulted in seventy positive (85.3 per cent) and twelve negative reactions.

This high percentage of successful vaccinations is understood when one recalls the efforts made to obtain potent virus. All vaccine was tried out on at least six patients before general use, and when the reactions were negative in over 25 per cent the vaccine was investigated for potency; if the vaccine was found lacking in that quality, the patients were revaccinated with good vaccine. There were a number of so-called potent vaccines received well before the date of expiration which gave a very small percentage of reactions. Three vaccines of such type and the reactions caused are outlined in table 1.

It will be noted that of 216 persons vaccinated, only forty-three gave positive reactions and 173 negative. When the persons with negative reactions were revaccinated with potent virus, all except six gave positive reactions, two of the latter being atypical. The inefficiency of these vaccines can also be ascertained from the reactions obtained with them when the vaccine was rubbed into the scarified eye of rabbits, as outlined in table 2, where it will be noted that in some instances vaccine virus, even as low as from one to twenty-five, did not produce a positive Paul reaction.[13]

COMMENT

Four patients had precipitous reactions, and within forty-eight hours had definite papulation that progressed to scabbing. Two of these reactions occurred six days after vaccination, and one, seven and nine days, after vaccination respectively.

Five persons (primaries) whom we could follow up did not have any local or general reaction after vaccination. They were vaccinated once a week for fifteen weeks without any reaction.

Colored patients who are vaccinated show a larger amount of pustulation to the same amount of vaccine virus than white patients. Vaccination is likewise more definite in that race, as in no instances in which colored patients were vaccinated intradermally (224 cases) were negative reactions obtained. Pustulation, likewise, occurs approximately a day earlier in colored patients.

One patient did not have any reaction seven days after vaccination. She was vaccinated again intradermally on the seventh day, without a reaction. Fourteen days after the first vaccination, she was vaccinated again. On the fifteenth day, the earliest vaccine injected began to have some local reaction, and there was a definite pustule by the twenty-second day. A reaction about the site of the second vaccination occurred on the twenty-first day, with pustulation on the twenty-seventh day, and a third reaction in the form of a nodule occurred about the site of the third injection on the twenty-sixth day; four days later a scab began to appear. Thirty-seven patients in the entire series had delayed reactions, that is, pustulation did not occur until from fourteen to twenty-one days after the injection of the vaccine.

Many authors say that fever does not occur when the method of intradermal vaccination is used. This has not been our experience, as practically all of our patients have had some fever starting as early as six days or as late as fourteen days after vaccination, and lasting from one to four days with systemic reactions often sufficient to cause the person vaccinated to go to bed and to cause a rise in temperature, in

13. Paul: A New Experimental Method with the Production of Variola-like Lesions on the Cornea of the Rabbit, Wein. klin. Wchnschr. **19**:996, 1916.

many cases as high as 104 F. In our experience, however, the fevr is of short duration, the majority of the patients having normal temperatures within twenty-four hours. There were eight cases of secondary infection with the formation of local abscesses.

Most persons who had been vaccinated previously showed an immunity reaction of induration and inflammation within twenty-four hours after vaccination, with absorption within seventy-two hours. Two patients, however, had an immediate allergic reaction without ready absorption and a nodular extension deep into the subcutaneous tissue and later formation of a scab without pustulation. Many of the patients previously vaccinated showed a hard, glassy papule within three or four days which did not pustulate, but which ruptured and was covered with a scab; healing occurred within from ten to fourteen days, leaving a minute scar. In a few of the patients, indurated nodules gradually appeared, beginning with the fourth day and lasting as long as twenty-one days, without any detectable formation of pus. One patient who had been successfully vaccinated in 1925, had a second definite positive reaction within a year when he was vaccinated by the skin method.

The smallness of the scab is not a good reason why the intradermal method should be adopted. In fact, from a standpoint of public health, the finding of scar tissue is the only definite proof of a successful vaccination. The advantages of this method might be enumerated thus: 1. There is less pain associated with this method, as the operator punctures once instead of scratching or puncturing several times. 2. A definite predetermined amount of vaccine can be injected, and none of the injected material is lost. The large sloughing of the secondarily infected ulcer which frequently follows the scratching methods is unusual in this type of vaccination. 3. This method can be used in certain skin diseases in which scratch methods or vaccination might be contraindicated, as in eczema, erysipelas and other conditions. 4. Playing children do not need to have a bandage to keep the dirt and infection out, as the skin automatically closes after the puncture by the needle, retaining the material, keeping out infection and cutting down the possibilities and discomforts of a sticky sore. 5. The intradermal method produces vaccinations in persons who previously have been unsuccessfully vaccinated, and a clear-cut reaction of immunity is much more easily obtained by this method in persons who previously have been vaccinated successfully. 6. The skin may be cleaned by any chemical before vaccination without killing the virus. 7. It is the best method for large groups from a time-saving standpoint.

The disadvantages of this method lie in the fact that it takes a little time to prepare vaccine material, but the advantages clearly outweigh this disadvantage. If a tuberculin syringe is used with a fine needle, the material may be sucked from the ordinary capillary vaccine tube and diluted by

drawing saline into the syringe. The second disadvantage is that vaccine may be delivered too deeply. This, of course, is possible, but since so many present day tests, such as tuberculin, Schick test, Dick test and others, are intradermal, every physician should be deft enough to carry out such a procedure.

CONCLUSION

Intradermal vaccination, in our experience, is the most efficient method of vaccination.

CHOLESTEROL AND LIPOID PHOSPHORUS IN INFANCY AND IN CHILDHOOD

NORMAL INCIDENCE IN CORD BLOOD AND DURING INFANCY AND EARLY CHILDHOOD *

MURRAY B. GORDON, M.D.

AND

DAVID J. COHN, PH.D.

BROOKLYN

The elaboration of newer methods for the determination of lipoids during the past few years has resulted in an increase in the literature on the subject; notwithstanding this added knowledge, the rôle played by these substances in the general body metabolism is neither clearly nor fully understood. One of the underlying reasons for this failure to evaluate properly the function of the lipoids is the insufficient data as to their normal incidence especially during infancy and childhood. Additional data on the normal values during these periods may be of some aid.

The collective term "lipoids" encompasses a heterogeneous mass of substances which are found after extraction of animal or vegetable tissue with ether or alcohol or a mixture of the two. Some of the substances obtained by extraction are fatty; they yield fatty acids on hydrolysis but differ from neutral fats in that they contain nitrogen or nitrogen and phosphorus; other substances do not bear any resemblance to fats except the accidental one of being soluble in ordinary fat solvents.

According to Aschoff,[1] the lipoids in the human body may be grouped into three classes: (1) the so-called phosphatids, including lecithin, cephalin and sphingomyelin; (2) phosphorus-free and nitrogen-containing substances such as the cerebrosides; (3) phosphorus-free and nitrogen-free substances, among which are cholesterol, fatty acids (oleic, palmitic and stearic), cholesterol fats, which are combinations of cholesterol and fatty acids, and, finally, neutral fats, which are combinations of fatty acids and glycerin. It may be mentioned that cholesterol is really a terpin alcohol of a complicated nature. Lecithin is a member of the lipoid phosphorus group.

Cholesterol and lecithin, or lipoid phosphorus, are amenable to fairly accurate quantitative determination by colorimetric methods which permit clinical application.

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* From the Pediatric Service and the Department of Laboratories, United Israel-Zion Hospital and the Department of Pediatrics, Long Island College Hospital.

1. Aschoff, L.: Lectures on Pathology, New York, Paul B. Hoeber, 1924,

Meigs, Blatherwick and Cary [2] investigated the variations in phosphoric acid compounds in pregnant and in lactating cows and in new-born calves; they found that the lipoid phosphorus is very low in the plasma of new-born calves and increases gradually until the animal is 1 year old. In pregnant cows, the lipoid phosphorus is lowered toward the end of pregnancy with a sudden rise after delivery and at the onset of lactation. The amount present in the cows was very much greater than that found in the calves.

Slemons and Stander [3] studied the lipoid phosphorus in the whole blood and plasma of simultaneously collected specimens of maternal and fetal blood at the time of delivery; they found that it is increased above the normal at the end of pregnancy, and that the maternal whole blood or plasma always contains a larger percentage of lipoids than the fetal.

Similar observations of a high lipoid phosphorus content in maternal and a low value in fetal blood were also obtained by Plass and Tompkins,[4] Mc Kellips, De Young and Bloor [5] and György.[6]

The blood of new-born infants contains a slightly lower amount of lipoid phosphorus than that of infants from 2 to 14 days old. Mc Kellips, De Young and Bloor,[5] who studied the cases of twenty-one normal infants between the ages of 5 and 26 days, reported a slightly higher average in the older infants, with marked individual variations.

The cholesterol content of both maternal and fetal blood at term was studied by Slemons and Stander,[3] who found a higher content in maternal blood. Rosenthal and Meier [7] also reported similar results.

György's investigations in 1926 [6] included a study of infants and older children. He reported eighty-seven normal cases; seventy-two infants were in the first year of life and the remainder were children between the ages of 2 and 13 years. His results are important, as he reported the largest number of observations made during the first year of life. He studied both the cholesterol and the lipoid phosphorus content and found low values for both at birth, with a general upward trend thereafter, the change being discernible as early as the first month.

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2. Meigs, E. B.; Blatherwick, N. R., and Cary, C. A.: J. Biol. Chem. **40**:469 (Dec.) 1919.

3. Slemons, J. M., and Stander, H. J.: The Lipoids of Maternal and Fetal Blood at the Conclusion of Labor, Bull. Johns Hopkins Hosp. **34**:7 (Jan.) 1923.

4. Plass, E. D., and Tompkins, E. H.: Placental Transmission: II. The Various Phosphoric Acid Compounds in Maternal and Fetal Serum, J. Biol. Chem. **56**:309 (June) 1923.

5. Mc Kellips, G. M.; De Young, I. M., and Bloor, W. R.: The Distribution of Phosphoric Acid in the Blood of Normal Infants, J. Biol. Chem. **47**:53 (June) 1921.

6. György, P.: Untersuchungen über Lipoide und Lipoidwirkungen bei Kindern, Jahrb. f. Kinderh. **112**:283-297 (May) 1926.

7. Rosenthal and Meier, quoted by György (footnote 6).

The object of our present study was the determination of the lipoid constituents of the blood in normal infants and in older children in an endeavor to confirm the results obtained by previous investigators and to arrive at normal valuations in ages not covered by them. With these observations as a basis, various pathologic conditions will later be investigated for any possible changes.

The first communication is based on a study of the cholesterol and lipoid phosphorus content as encountered under normal conditions in cord blood from the umbilical cord at birth, and from the blood of infants in the first week of life and of children up to the age of 6 years. For comparative purposes, we also include personal observations on the blood of pregnant women at various stages of gestation.

The material for study was obtained from the following sources: pregnant women attending the antenatal clinic of the hospital, 16; cord blood at the time of delivery, 16; infants in the hospital nursery in the first week of life, 16; older infants and children from the Infants Home of Brooklyn (an orphan asylum): from 6 months to 1 year of age, 7; from 1 to 6 years of age, 32. It is our priviledge to be able to report the largest number of normal lipoid values in children from 1 to 6 years of age, as the only other observer of this age period (György) included only six children between these ages.

Lipoid determinations may be made on whole blood, plasma or serum. A comparison of the results of the various investigators shows that there is little difference between the lipoid content of plasma and of serum. Our observations were made on the content of the blood serum.

The method used was as follows: From 3 to 5 cc. of blood is drawn by venipuncture, preferably from the median basilic vein, and is allowed to stand until the serum separates. As soon as possible after that, 1 cc. of serum is added, drop by drop, to 15 cc. of an alcohol-ether mixture containing 75 per cent of alcohol and 25 per cent of ether. This precipitates the protein into fine flakes; the finer the flakes, the more complete the reaction. The mixture is brought to a boil in a water bath, cooled and enough alcohol-ether added to bring the total volume to 25 cc. The proteins are filtered off, giving a clear substance which contains the total alcohol-ether fraction of the serum, including both cholesterol and the phosphorus-bearing lipoids.

For the determination of cholesterol, 10 cc. of this filtrate is treated according to the method of Bloor [8] and another 10 cc. is examined for its phosphorus content by the Briggs-Bell-Doisy method.[9]

Any comparison of the results obtained in the determination of lipoid phosphorus or lecithin must take into consideration the form in

8. Bloor, W. R.: Determination of Cholesterol in Blood, J. Biol. Chem. **24**: 227, 1916.

9. Briggs, J. Biol. Chem. **53**:13, 1922; **59**:255 (March) 1924.

which the reports are expressed. Results are reported in the literature in one of three ways: "as phosphorus," "as phosphoric acid" or "as lecithin." This is confusing, as it prevents proper comparative interpretations of the various observations unless the results are expressed in uniform terms. To permit comparison with the results obtained by György, whose observations cover the same age period, we have followed his methods of investigation, making our calculations on the basis of phosphorus, and designating as "lipoid phosphorus" the entire phosphorus-containing fraction of the serum which is soluble in the mixture of alcohol and ether. Our results are expressed in milligrams of phosphorus per hundred cubic centimeters of serum. For comparative purposes, observations of other investigators may be converted to the same phosphorus basis as follows: Amounts expressed in terms of phosphoric acid are multiplied by the factor 31/98. When lecithin as

TABLE 1.—*Cholesterol and Lipoid Phosphorus Content in Cord Blood Serum*

No.	Cholesterol, Mg. per 100 Cc.	Lipoid Phosphorus, Mg. per 100 Cc.	No.	Cholesterol, Mg. per 100 Cc.	Lipoid Phosphorus, Mg. per 100 Cc.
1	80	3.8	9	90	4.3
2	105	4.6	10	75	3.8
3	95	4.2	11	90	4.0
4	90	4.4	12	85	3.7
5	85	4.0	13	100	4.2
6	70	3.9	14	95	5.0
7	100	4.9	15	80	3.6
8	85	3.8	16	100	3.9
Average				89	4.1

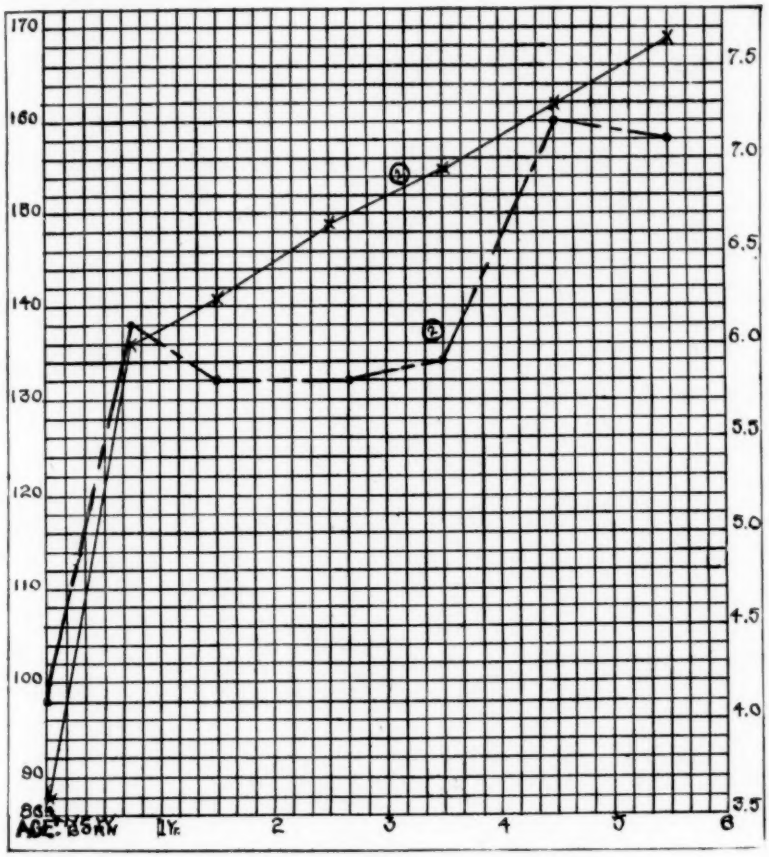
such is reported, the phosphorus content may be obtained by taking 4 per cent of the given figure, this being the average amount of phosphorus found in analyses of lecithin.

It is a well known fact that under normal conditions the physiologic incidence of any substance is found within a zone of marked variations instead of along a straight line. We found this to be true also of the values obtained in this investigation. Because of this large physiologic variation even in normal persons, any study of normal valuations must necessarily deal with averages, and we have therefore based the curves we have plotted on the averages instead of on the individual figures. In evaluating our curves, it must be borne in mind that they are subject to the faults attending work with averages.

Tables 1 to 4 show in detail the cholesterol and lipoid phosphorus content in blood serum. The chart represents the averages at the different age periods under investigation.

The lowest values are found in the cord blood. The amount of lipoid phosphorus found by us (4.1 mg. per hundred cubic centimeters) corresponds to that obtained by Plass and Tompkins [4] and by György.[6]

This value represents the content of lipoid phosphorus in the new-born under normal conditions. The first week of life evidently does not produce much change, as shown by the presence of practically the same amount (4.2 mg. per hundred cubic centimeters) Mc Kellips, De Young and Bloor,[5] who studied the plasma content, reported 4.6 mg. per hundred cubic centimeters as the average for infants from 2 to 26 days old.



Graphic illustration showing the cholesterol and lipoid phosphorus content in blood serum of children at different ages. 1 represents the variation of cholesterol content per hundred cubic centimeters; 2 represents the lipoid content per hundred cubic centimeters.

György [6] gave 6.3 mg. per hundred cubic centimeters as the average for the first month of life, but he did not state the exact age of the infants in days. His investigations may include a larger number of infants nearer the end of the one month period, which would explain the greater lipoid phosphorus content obtained by him.

We did not have an opportunity to investigate the conditions present in the blood serum of infants between the ages of 1 week and 6 months. As our observations at birth and within the first week approximate those obtained by others, it is fair to assume that our results for other age periods may be accepted as normal. There is a marked rise in the lipoid phosphorus in infant's blood up to the first year, and then there is apparently a stationary level for the next four years; finally, a rise occurs between the ages of 4 and 6 years.

TABLE 2.—*Cholesterol and Lipoid Phosphorus Content in Infants' Blood Serum in First Week*

No.	Cholesterol, Mg. per 100 Cc.	Lipoid Phosphorus, Mg. per 100 Cc.	No.	Cholesterol, Mg. per 100 Cc.	Lipoid Phosphorus, Mg. per 100 Cc.
1	85	3.9	9	90	4.3
2	85	4.4	10	95	4.5
3	80	3.7	11	75	3.6
4	80	3.9	12	80	4.3
5	100	4.6	13	80	4.1
6	105	5.0	14	80	3.8
7	95	4.8	15	85	3.9
8	90	4.0	16	90	4.5
Average				87	4.2

TABLE 3.—*Cholesterol and Lipoid Phosphorus Content in Blood Serum of Older Children*

Age	Sex	Cholesterol, Mg. per 100 Cc.	Lipoid Phosphorus, Mg. per 100 Cc.	Age	Sex	Cholesterol, Mg. per 100 Cc.	Lipoid Phosphorus, Mg. per 100 Cc.
6 mo. 3 wk.	F	125	6.9	2 yr. 5 mo.	M	155	3.9
7 mo.	M	110	4.9	2 yr. 5 mo.	M	145	6.2
7 mo. 1 wk.	F	180	7.1	2 yr. 9 mo.	F	135	3.5
9 mo.	M	110	4.1	3 yr.	M	145	5.5
10 mo. 3 wk.	M	175	8.2	3 yr.	F	175	6.5
11 mo. 3 wk.	F	115	5.3	3 yr. 2 mo.	M	120	6.0
1 yr. 2 mo.	F	140	6.2	3 yr. 5 mo.	M	155	5.5
1 yr. 6 mo.	F	135	6.4	3 yr. 7 mo.	M	180	6.2
1 yr. 6 mo.	M	145	5.7	4 yr. 2 mo.	F	130	6.3
1 yr. 7 mo.	F	170	8.1	4 yr. 3 mo.	M	175	8.9
1 yr. 7 mo.	M	155	4.8	4 yr. 6 mo.	M	140	7.3
1 yr. 8 mo.	M	110	4.6	4 yr. 7 mo.	F	190	6.8
1 yr. 9 mo.	M	140	5.7	4 yr. 8 mo.	M	150	5.1
1 yr. 9 mo.	F	135	5.3	4 yr. 11 mo.	M	160	8.4
1 yr. 10 mo.	F	140	5.8	4 yr. 11 mo.	F	190	7.6
2 yr. 1 mo.	M	135	7.5	5 yr. 2 mo.	F	160	5.9
2 yr. 2 mo.	M	170	6.6	5 yr. 6 mo.	F	175	6.9
2 yr. 3 mo.	F	130	7.2	5 yr. 6 mo.	F	160	6.4
2 yr. 5 mo.	F	170	5.3	6 yr. 2 mo.	M	180	8.2

The cholesterol values show a more general tendency to a gradual increase than those of lipoid phosphorus forming a more even curve. The lowest values are also found in cord blood and during the first week. Our observations on the blood of the umbilical cord (89 mg. per hundred cubic centimeters) are a trifle higher than those obtained by György (79 mg. per hundred cubic centimeters), but they are much lower than the results reported by Slemons and Stander [3] and Slemons and Curtis [10]

10. Slemons, J. M., and Curtis, C. S.: Cholesterol in Blood of Mother and Fetus (A Preliminary Note) Am. J. Obstet & Gynec. **75**:569 (April) 1917.

(115 to 225 mg. per hundred cubic centimeters). After the first week, there is a gradual but steady rise in the cholesterol content, which reaches 169 mg. per hundred cubic centimeters at the sixth year. Our average for the period between the second and sixth year, based on thirty-two determinations, is 155 mg. per hundred cubic centimeters, while György's is 173 mg. per hundred cubic centimeters based on six observations. A comparison of his series and ours demonstrates the gradual

TABLE 4.—*Cholesterol and Lipoid Phosphorus Content in Blood Serum of Pregnant Women*

Month of Gestation	Cholesterol, Mg. per 100 Cc.	Lipoid Phosphorus, Mg. per 100 Cc.	Month of Gestation	Cholesterol, Mg. per 100 Cc.	Lipoid Phosphorus, Mg. per 100 Cc.
8th	310	12.8	9th	265	9.2
7th	250	7.4	7th	285	10.0
9th	280	11.4	6th	260	8.7
7th	235	8.2	5th	195	6.7
5th	210	6.8	8th	375	11.6
5th	190	8.0	3d	170	7.4
5th	280	8.3	5th	230	8.1
9th	255	11.5	5th	245	8.4
Average				252	9.3

TABLE 5.—*Normal Incidence of Cholesterol and Lipoid Phosphorus in Infancy and Childhood* *

Age	Cholesterol		Lipoid Phosphorus	
	György	Gordon and Cohn	György	Gordon and Cohn
Cord	79	89	4.1	4.1
1st week	...	87	...	4.2
1st month	122	...	6.3	...
2d month	127	...	6.4	...
3d month	138	...	6.2	...
4th month	154	...	6.2	...
5th-12th month	158	136	6.5	6.1
1st-2d year	...	141	...	5.8
2d-3d year	...	149	...	5.8
3d-4th year	...	155	...	5.9
4th-5th year	...	162	...	7.2
5th-6th year	...	169	...	7.1
2d-6th year	173	155	7.8	6.5
6th-13th year	190	...	6.2	...

Other Observers—Plass and Tompkins: Newborn, lipoid phosphorus, 4.1 mg.
Mc Kellips, De Young and Bloor: 2-23 days, lipoid phosphorus, 4.6 mg.

* Expressed in mg. per 100 cc. of cholesterol and phosphorus, respectively.

increase in cholesterol from birth up to the sixth year in our series and up to the thirteenth year in his.

The highest values for both cholesterol and lipoid phosphorus were found in the blood serum of pregnant women, which confirmed the results obtained by others. In our series, the values increased with the term of pregnancy, the highest figures being found in the eighth month.

The question of the so-called lipoid quotient will be considered in a subsequent communication.

SUMMARY AND CONCLUSIONS

Serum obtained from blood of the umbilical cord at birth, and from the blood of infants during the first week of life and of children from 6 months to 6 years of age was studied for its cholesterol and lipoid phosphorus content. Similar studies were also made on blood serum from pregnant women. Tables and curves are presented showing the normal incidence during these periods.

The cholesterol curve shows the lowest values at birth and during the first week, a sharp rise in the first year and a gradual tendency to rise thereafter until the sixth year. The curve of the lipoid phosphorus content is similar to that of cholesterol but not as even. The lowest lipoid phosphorus values are found in the cord blood, practically without change, during the first week of life; there is a marked rise in the first year, an apparent level for the next four years and finally a rise from the fourth to the sixth year. The highest values for both cholesterol and lipoid phosphorus are found in the blood of pregnant women.

THE URINARY LEUKOCYTE COUNT IN CHILDREN IN NORMAL AND IN PATHOLOGIC CONDITIONS *

LEO S. FRIEDMAN, M.D.
AND
A. GRAEME MITCHELL, M.D.
CINCINNATI

There is a lack of uniformity in the methods of quantitative estimation of leukocytes in the urine, and considerable difference of opinion prevails concerning the normal number of these cellular elements. Pflaumer,[1] Hill,[2] Dyson,[3] Dingwall-Fordyce [4] and Amberg [5] agree that normal urine, that is, urine of healthy children, may contain pus cells, but they do not offer any opinion as to what constitutes a normal maximum. Helmholz [6] believes that the uncentrifugalized urine of boys should contain not more than 2 or 3 cells per low-power field, and that of girls not more than from 6 to 8. For some time, we have been interested in this matter and have felt that the number of leukocytes in the urine has diagnostic and prognostic value.[7] The present study is an attempt to define normal and pathologic urine of children in terms of the cell content per cubic millimeter.

The method employed was one mentioned by Roth,[8] Block and Nyum [9] and Dyson.[3] The thoroughly mixed, fresh, undiluted urine was examined, and the number of cells per cubic millimeter was determined by means of a blood counting chamber. The high power of the microscope was employed to distinguish leukocytes from small round epithelial cells. This was usually easy to do, although some authors,

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* From the B. K. Rachford Department of Pediatrics, College of Medicine, University of Cincinnati.

1. Pflaumer, E.: Zentralbl. f. Chir. **50**:585, 1923.

2. Hill, L. W.: Review of the Literature of 1920 on Genito-Urinary Conditions in Children, Am. J. Dis. Child. **22**:417 (Oct.) 1921.

3. Dyson, J. E.: M. Clin. North America **3**:1547, 1920.

4. Dingwall-Fordyce, A.: Brit. M. J. **1**:97, 1922.

5. Amberg, S., in Abt: Pediatrics, Philadelphia, W. B. Saunders Company, 1924, vol. 4, p. 1032.

6. Helmholz, H. F., in Abt: Pediatrics, 1924, vol. 4, p. 914.

7. Mitchell, A. G.: Arch. Pediat. **40**:747, 1923. Griffith, J. P. C., and Mitchell, A. G.: The Diseases of Infancy and Childhood, ed. 2, Philadelphia, W. B. Saunders Company, 1927, vol. 2, p. 469.

8. Roth, L. J.: California State J. Med. **20**:5, 1922.

9. Block, E. B., and Nyum, K.: South. M. J. **9**:972, 1916.

such as Addis,[10] believe it is practically impossible to differentiate the two types of cells. At any rate, epithelial cells are seldom present in such numbers as materially to affect the count. Clumping of the leukocytes may largely be obviated by thorough agitation of the specimen. The value of this method lies in the fact that it conveys at once an accurate idea of the actual number of pus cells in any given specimen; it enables several examiners to compare counts at different times from the same case; finally, it furnishes a prognostic as well as a diagnostic aid by establishing an increase or decrease in the counts. This method does not, of course, take into consideration the factors of total volume of urine and concentration. It is, however, a more accurate method than the estimation of the number of cells per high-power field in a smear of variable thickness.

About 530 determinations were made on the urine of infants and children ranging in age from a few weeks to 13 years, the results being classified as in the following paragraphs. Specimens were obtained in the ordinary way without special precautions. Cases in which vaginitis was present were excluded. Catheter specimens were obtained in selected cases for comparison with voided specimens. All figures refer to the number of cells per cubic millimeter.

CLASSIFICATION OF CHILDREN AND INFANTS ACCORDING TO DISEASES PRESENT

Group I: Normal.

Apparently healthy infants and children with normal temperatures, and free from evidence of infection or genito-urinary disturbances.

Group II: Respiratory Infections.

Children with pneumonia, tonsillitis, cervical adenitis and otitis media.

(*a*) Acute or febrile stage.

(*b*) Subacute or afebrile stage.

Group III: Dehydration (Enteritis).

(*a*) Febrile stage.

(*b*) Afebrile stage.

Group IV: Miscellaneous Infections with Fever.

Including children with furunculosis, meningitis, typhoid fever and arthritis.

Group V: Pyelitis.

Group VI: Nephritis.

In addition to the foregoing grouping, the cases were divided into two age classes, those below and those above 2 years; they were also studied according to sex.

Group I: Normal (140 Counts).—The average count for both sexes and all ages was 10. Twenty per cent did not reveal any cells, while 90 per cent showed 20 or less cells. Seven per cent had from 20 to 40 cells. In the infants, the average count was practically the

10. Addis, T.: J. Clin. Investigation **2**:409, 1926.

same for both sexes (12 cells), while the average count was greater in female (12 cells) than in male (7 cells) for those children above 2 years of age.

Catheter specimens contained about the same number of cells as voided specimens.

Group II: Respiratory Infections.—(*a*) Acute Stage (145 Counts): The urine of children suffering from various acute respiratory infections contained a considerably greater number of pus cells than the normal specimens. The average count in infants was 22 for girls and 19 for boys; and 52 for girls and 31 for boys over 2 years of age. Thirty-one per cent of specimens from females and 22 per cent from males contained over 40 cells, while no specimens were entirely free from cells. In this and the remaining groups, catheter specimens in the older girls differed in cell content from voided specimens but not to a marked degree. (*b*) Subacute Stage (34 Counts): The counts in general approached those of the normal group, with the exception of those of the older girls, in whom they were somewhat higher. In the infants, the average count was 16 for girls and 12 for boys, while for those above 2 years of age it was 33 for girls and 4 for boys.

Group III: Dehydration (Enteritis).—(*a*) Febrile Stage (30 Counts): In the female the counts ranged between 23 and 900 with an average of 236, while in the male they varied from 0 to 43 with an average of 20. Cell counts over 40 were found in 21 per cent of females and 7 per cent of males.

In accordance with the usual experience, the diagnosis of a coexisting pyelitis was made in many of these cases. Schiff and Bayer [11] and Faerber and de Boutenard [12] consider that dehydration and concentration of urine are the etiologic factors responsible. (*b*) Afebrile Stage (30 Counts): In these cases, cell counts ranging from 3 to 350 averaged 75 in the female and 53 in the male. After the acute stage had subsided, there was often evidence of pyuria.

Group IV: Miscellaneous Infections with Fever (72 Counts).—Under 2 years of age, the counts in the female varied from 11 to 85 with an average of 36; in the male, from 5 to 65 with an average of 23. Above 2 years of age, an average of 55 in females and 15 in males was found. The specimens in 8 per cent of the females and in 10 per cent of the males were free from cells.

In general, the results here were much like those in groups II (*a*) (respiratory infections with fever).

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11. Shiff, E., and Bayer, W.: Jahrb. f. Kinderh. **108**:157, 1925.
12. Faerber and de Boutenard: Jahrb. f. Kinderh. **113**:259, 1926.

Group V: Pyelitis (50 Counts) and *Group VI: Acute Nephritis* (31 Counts).—These groups included children with acute and chronic cases of definite infection of the genito-urinary tract unassociated with disease elsewhere. The counts were sufficiently above the upper limit of normal to obviate any difficulty in classification. Repeated counts were of particular value in following the course of the disease.

SUMMARY AND CONCLUSIONS

1. The urine of apparently healthy infants and children contained an average of 10 pus cells per cubic millimeter. Ninety per cent of the urine showed 20 cells or less. The upper limit of normality for all ages was 40, counts of from 20 to 40 being present more often in girls of the older age groups.

Between the ages of 2 and 13, the urinary leukocyte counts averaged 13 per cubic millimeter for girls and 7 for boys; under 2 years of age, the counts were approximately equal in both sexes.

2. The urine of infants and children suffering from various respiratory, intestinal or other infections frequently showed a varying degree of pyuria in excess of the normal. The leukocyte counts tended to be higher in the older age group than in the younger, higher in girls than in boys and higher in the acute than in the subacute or afebrile stage.

3. In cases of pyelitis and nephritis, the counts were definitely higher than in any other conditions studied.

4. Leukocyte counts in the urine which show more than 20 but less than 40 cells per cubic millimeter are suggestive of urinary infection but may readily occur in concentrated urine and in acute febrile diseases. Leukocyte counts of over 40 per cubic millimeter point strongly to infection somewhere along the urinary tract if vaginitis has been excluded.

5. When large amounts of pus appear in the urine, the diagnosis is obvious, but in early or doubtful cases the estimation of the number of cells is often of great value.

THE EFFECT OF THYROID THERAPY ON CHILDREN *

ANNE TOPPER, M.D.
AND
PHILIP COHEN, M.D.
NEW YORK

Thyroid extracts are known for their effect on metabolism. Not only is the weight curve affected, but there is a greater excretion of water, salts and nitrogen, and growth and regeneration are promoted. This is most strikingly seen in the cretin or myxedematous patient. Associated with these metabolic changes is the elevation of the basal metabolic rate from a low to a normal level.

Before the advent of tests of basal metabolism, the effects of thyroid action were judged more or less clinically; that is, by improved mentality, increased irritability, decreased sluggishness and alterations in growth phenomena. Today, however, the association between studies of basal metabolism and of thyroid disease is so close that many consider scientific proof of thyroid disease lacking unless an abnormal basal metabolic rate has been demonstrated.[1]

As a corollary to this close association, the general impression has been that even in normal persons, exhibition of thyroid extract is attended with increased basal metabolism, and the basal metabolic rate is used as the criterion of a positive effect of the thyroid therapy.

This paper deals with the effect of thyroid therapy on normal children and on a small series of children showing hypothyroidism.

Some time ago, we had occasion to use thyroid therapy on some patients with nephrosis, as it has been highly recommended and strenuously urged in the treatment of this condition.[2] Since the modern conception of nephrosis is that it is a general metabolic disease and not a renal disease, we were willing to study the rôle of the thyroid gland in this disease and to test the effect of thyroid therapy. Accordingly, we studied the basal metabolism in these cases and then studied the effect of thyroid therapy as judged by the basal metabolism, a criterion which, from the observations of previous observers and experimenters,

* Received for publication, Nov. 21, 1927.

* From the Pediatric Service of Mount Sinai Hospital.

1. DuBois, E. F.: Basal Metabolism in Health and Disease, Philadelphia and New York, Lea and Febiger, 1924, p. 294. Kessell, L.; Hyman, H. T., and Lande, H.: Studies of Exophthalmic Goiter and the Involuntary Nervous System, Arch. Int. Med. **31**:433 (March) 1923.

2. Eppinger: Zur Pathologie und Therapie des Menschlichen Odema, Berlin, 1917. Epstein, A. A.: Thyroid Therapy and Thyroid Tolerance in Chronic Nephrosis, J. A. M. A. **87**:913 (Sept.) 1926.

we felt was a reliable guide to the effect of thyroid therapy. To our surprise, a change in the output of heat did not occur unless an infection supervened.

We extended our studies, then, to other children, with and without metabolic abnormalities. Our procedure, which we were able to follow with few exceptions, which will be noted, was as follows:

Each child was kept in bed during the study, and his diet remained unchanged for this period. The basal metabolism was determined on several occasions, until we were certain that a normal reading had been obtained. The respiratory apparatus used was the Krogh machine, which we knew to be accurate from previous experiments and tests. All determinations were performed in duplicate or triplicate, and the usual postabsorptive period and required rest before testing were always observed. Thyroid therapy was begun after a normal basal metabolism reading had been obtained. We began with thyroid extract, ¼ grain (0.16 Gm.) three times daily. The preparation used was Burroughs Welcome, a reliable one, which had been standardized according to its iodine content and which had been proved to be an excellent index of the activity of the glandular extract.[3] Furthermore, our studies showed the preparation to be a potent one, as certain cases showed an increased basal metabolism after the exhibition of the extract. After the small dose of thyroid was given for a few days, the dosage was gradually increased to 1, 2, 3 and 5 grains (0.06, 0.13, 0.19 and 0.32 Gm.) three times daily, but only after the test of the basal metabolism had been performed before each change in dosage. We felt that if 15 grains (0.97 Gm.) daily was inefficacious, then a further increase in the dosage in the treatment of children would be futile and would not yield useful information. Cretins and myxedematous patients need far less thyroid to bring them to a normal state.[4]

In the beginning, we tried other extracts if our stock preparations did not produce an increase in metabolism. In cases in which the thyroid extract seemed ineffective, thyroxin was given intravenously in doses of 4 or 5 mg., a good sized dose for a child. The basal metabolism was studied for two weeks after the injection in these cases, because of the well known delayed effect of thyroxin. In some cases, we repeated the injection of thyroxin. In one case, we gave thyroxin intravenously on the same day that the child received 12 grains (0.78 Gm.) of thyroid extract orally. We felt fairly safe in doing this, because of the apparent delay in the action of thyroxin, although we were aware that the action of thyroid extract lasted for two or three weeks.

3. Hunt, R.: Standardization of Thyroid Preparations, Arch. Int. Med. **35**: 671 (June) 1925.

4. Means, J. H., and Aub, J. C.: The Basal Metabolism in Hypothyroidism, Arch. Int. Med. **24**:404 (Oct.) 1919. Janney, W. W.: Studies in Thyroid Therapy, Arch. Int. Med. **22**:187 (Aug.) 1918.

Under these conditions, we carefully studied the effect of thyroid on the metabolism of eight children. In addition, we also noted the pulse rate, weight, diuresis, nervous changes and gastro-intestinal reactions. Changes in growth could not adequately be studied in these cases, either because the period of study was too short for these effects to be noted or because the illness of the patient would preclude growth.

In order to obtain the effects on more nearly normal children, we studied the effect of thyroid extract on six children in the dispensary. The basal metabolism, weight and height were studied over a relatively long period, so that the question of growth could be better investigated. Because these patients were ambulatory, other factors, such as diet, pulse rate and diuresis could not be carefully studied, but were controlled as far as possible at the periods of observation. Metabolic determinations were performed strictly according to the technic previously described. Descriptions of the cases are given in the tables.

TABLE 1.—*Effects of Thyroid Therapy in Case 1* *

B. D., a girl, aged 7: surface area, 0.9 sq. m.; sitting height, 65 cm.; total height, 118 cm.; diagnosis, nephrosis; diet, 1,400 calories, 13 per cent protein.

Date, 1926	Weight, Kg.	Pulse	Total Calories	Comment
Feb. 17	26.6	108	864	Marked edema
18	26.6	100	951	Began thyroid, ¼ grain (0.01 Gm.) three times daily
22	27	96	871	Increased thyroid to 3 grains daily
23	27.5	96	881	
27	24.4	96	871	Edema disappearing
March 2	22.5	90	866	
5	22	96	857	
9	21.7	78	857	Edema markedly decreased
16	22.9	124	1,073	Temperature, 101; erysipeloid infection of leg
17	23			
26	25.8	124	1,063	Temperature, 100; edema increasing
28	....	...	.....	Thyroid, 4½ grains (0.29 Gm.) daily
April 5	26	80	860	
12	26.9	90	870	Thyroid, 6 grains (0.4 Gm.) daily
16	22	100	1,046	Temperature, 101; erysipeloid infection
21	....	...	.....	Thyroid, 9 grains (0.6 Gm.) daily
26	20	96	874	Edema gone
30	20	96	864	
May 15	21.8	92	871	Thyroid stopped
19	23	112	938	Edema reappearing
24	24.5	100	931	
26	24.6	100	946	
June 5	25.5	100	946	Thyroxin, 5 mg. intravenously
7	26	94	879	
8	26.5	102	886	
11	26	100	881	
14	26	100	881	
16	26	96	888	
24	26.8	110	883	Edema marked; thyroxin, 5 mg.
26	26	110	871	
28	25.3	102	976	Temperature, 100; red throat
30	24	98	864	
July 2	24	96	862	
3	23.6	84	864	
6	23	100	878	Edema decreasing

Standards of Metabolism†		Deviation from Standard
Pirquet	845 calories	Plus 2 per cent
Weight	902	Minus 10 per cent
Surface area	875	Minus 1 per cent
Height	847	Plus 2 per cent

* Thyroid therapy did not influence basal metabolism or cause any untoward physiologic reactions. There was no constant relation between the edema and thyroid therapy.

† Standards of metabolism:

Pirquet: An Outline of the Pirquet System of Nutrition, Philadelphia, W. B. Saunders Company, 1922.

Weight: Benedict, F. G., and Talbot, F. B.: Metabolism and Growth from Birth to Puberty, Carnegie Inst. Washington, 1921, pub. 362, pp. 140, 142 and 179.

Surface area: Ibid. pp. 161, 164 and 180.

Height alone: Talbot, F. B.: Basal Metabolism in Children, Physiol. Rev. 5: 477 (Oct.) 1925.

TABLE 2.—*Effects of Thyroid Therapy in Case 2* *

M. L., a boy, aged 5½: surface area, 0.8 sq. m.; sitting height, 62 cm.; height, 115 cm.; diagnosis, nephrosis; diet, 1,500 calories, 13 per cent protein.

Date, 1926	Weight, Kg.	Pulse	Total Calories	Comment
March 25	20	70	860	Patient had been getting thyroid orally, 3 grains daily since February 19; metabolism tests not made
26	20	72	876	No clinical symptoms No edema
April 16	20	74	857	
30	20	76	866	
May 15	21	72	871	Thyroid stopped
19	21	76	866	
24	22	72	871	
26	22	70	881	
June 5	22.3	70	881	Thyroxin, 4 mg. intravenously
6	22	72	890	
8	22	74	850	
10	22	74	868	
11	21.9	74	878	
15	21.6	74	866	

Standards of Metabolism		Deviation from Standard
Pirquet	768 calories	Plus 10 per cent
Weight	860	None
Surface area	850	Minus 1 per cent
Height	875	None

* Thyroid therapy had no influence on basal metabolism, pulse rate, weight, nervous or gastro-intestinal systems.

TABLE 3.—*Effects of Thyroid Therapy in Case 3* *

C. O., a girl, aged 12: surface area, 1.2 sq. m.; sitting height, 75 cm.; height, 144 cm.; diagnosis convalescing from acute rheumatic fever; diet, 2,500 calories, 13 per cent protein.

Date, 1926	Weight, Kg.	Pulse	Total Calories	Comment
				Symptom-free since June 6
June 23	31.5	94	1,121	Thyroxin, 5 mg. intravenously
24	31.5	92	1,097	
26	32	90	1,114	
28	32	90	1,110	
30	32	90	1,106	
July 1	31.5	94	1,130	
2	31.5	94	1,106	
3	31.5	94	1,106	
6	31.5	94	1,097	

Standards of Metabolism		Deviation from Standard
Pirquet	1,125 calories	Minus 2 per cent
Weight	1,080	Plus 1 per cent
Surface area	1,150	Minus 4 per cent
Height	No figures available	

* Thyroid therapy had no effect on basal metabolism, and apparently caused no physiologic alterations.

TABLE 4.—*Effects of Thyroid Therapy in Case 4* *

R. C., a boy, aged 9: surface area, 0.85 sq. m.†; sitting height, 68 cm.†; height, 130 cm.†; diagnosis, myositis ossificans; diet, 2,000 calories, 13 per cent protein.

Date, 1926	Weight, Kg.	Pulse	Total Calories	Comment
June 22	18.5	90	984	Thin, emaciated boy
23	....	...	980	
24	....	...	984	Thyroxin, 5 mg. intravenously
26	....	...	989	
28	....	...	979	
30	....	...	984	
July 2	....	...	986	
3	....	...	1,000	
6	....	...	984	
9	....	...	979	

Standards of Metabolism		Deviation from Standard
Pirquet	924 calories	Plus 6 per cent
Weight	818	Plus 20 per cent
Surface area	900	Plus 9 per cent
Height	1,045	Minus 6 per cent

* Thyroid therapy had no effect on basal metabolism and apparently caused no physiologic alteration.

† All measurements approximate because of partial ankylosis of elbows and knees.

TABLE 5.—*Effects of Thyroid Therapy in Case 5* *

L. B., a girl, aged 8: surface area, 1.2 sq. m.; sitting height, 77 cm.; height, 140 cm.; diagnosis, petit mal, no significant neurologic symptoms; diet, 2,500 calories, 13 per cent protein.

Date, 1926	Weight, Kg.	Pulse	Total Calories	Comment
				Obese, overnourished child
June 17	44.3	68	1,632	Appetite poor; refused food
18	....	...	1,577	
19	....	...	1,576	
24	....	...	1,550	
26	42.6	...	1,584	
July 3	42	...	.....	Thyroid, 1½ grains (0.09 Gm.) daily
5	....	...	1,582	Thyroid, 3 grains (0.19 Gm.) daily
7	42	...	1,547	Thyroid, 6 grains daily
9	42	...	1,502	Thyroid, 9 grains daily
11	41.6	...	1,548	Thyroid, 15 grains daily
13	....	...	1,500	
14	41	60	1,493	
15	....	60	1,480	
16	41	60	1,445	Stopped thyroid

Standards of Metabolism		Deviation from Standard	
Pirquet	1,095 calories	Plus 20 per cent	Obesity on a nutritional basis
Weight	1,135	Plus 20 per cent	
Surface area..	1,180	Plus 39 per cent	
Height	No figures available		

* Thyroid therapy had no apparent effect on basal metabolism, which, with the weight, decreased before therapy was started, because of partial inanition from poor appetite and small amount of food eaten. Thyroid did not cause physiologic alteration; the slow pulse with decrease in basal metabolism should be noted.

TABLE 6.—*Effects of Thyroid Therapy in Case 6* *

A. S., a boy, aged 12: surface area, 1.2 sq. m.; sitting height, 79 cm.; height, 147 cm.; diagnosis, convalescing from acute rheumatic fever; diet, 2,500 calories, 13 per cent protein.

Date, 1926	Weight, Kg.	Pulse	Total Calories	Comment
Nov. 6	36	76	1,214	Symptom-free since October 30
7	....	...	1,228	Thyroid, 3 grains daily
11	35.9	...	1,238	Thyroid, 6 grains daily
12	35.7	...	1,248	
13	....	80	1,276	
16	....	...	1,224	Thyroid, 9 grains daily
20	....	...	1,224	Thyroid, 12 grains daily
24	....	...	1.224	
26	35	...	.....	Thyroxin, 5 mg. intravenously
27	33.8	124	1,460	Increased diuresis; tremor; dizziness
28	33.8	100	1,245	
Dec. 1	33.8	70	1,106	
3	33.8	78	1,248	
4	....	70	1,150	Patient discharged
March 5	....	70	1,272	In dispensary; no thyroid since November 27

Standards of Metabolism		Deviation from Standard
Pirquet	1,217 calories	None
Weight	1,240	Minus 2 per cent
Surface area	1,200	None
Height	1,242	Minus 2 per cent

* Thyroid therapy had an effect only when thyroxin was given synchronously with 12 grains (0.78 Gm.) of thyroid extract. There was an increased basal metabolism (plus 15 per cent), increased pulse rate, diuresis and tremor — all only for from one to two days. This patient was subnormal mentally. He had been tested in our Mental Hygiene Clinic, showing an intelligence quotient of 78, with a mental age of 8/7. Under thyroid administration, he appeared markedly more alert and mentally responsive, although additional mental tests did not bear out the apparent clinical improvement.

TABLE 7.—*Effects of Thyroid Therapy in Case 7* *

B. S., a girl, aged 9: surface area, 1 sq. m.; sitting height, 68 cm.; height, 126 cm.; diagnosis, fever of unknown origin, 11 weeks duration, obesity, hypothyroidism; diet, 1,500 calories, 13 per cent protein.

Date, 1926	Weight, Kg.	Pulse	Total Calories	Comment
July 20	34	60	744	No clinical symptoms; temperature, 100
21	..	..	748	
22	..	..	...	Thyroid, 1½ grains daily
24	..	68	768	Thyroid, 3 grains daily
27	..	..	...	Thyroid, 4½ grains daily
30	..	70	...	Thyroid, 6 grains daily
Aug. 3	33	78	840	Thyroid, 9 grains daily
10	32	80	1,030	Stopped thyroid
12	30	80	972	
20	30	80	1,080	
March 5	..	80	1,144	In dispensary
12	..	80	1,219	In dispensary

Standards of Metabolism		Deviation on Admission	On Discharge
Pirquet	925 calories	Minus 20 per cent	Plus 14 per cent
Weight	1,124	Minus 32 per cent	Minus 4 per cent
Surface area	980	Minus 24 per cent	Plus 9 per cent
Height alone	925	Minus 20 per cent	Plus 14 per cent

* This child ran a temperature of from 100 to 101 all during his stay in the hospital, with no discoverable cause. Child had clinical manifestations of hypothyroidism and a low basal metabolic rate. Under thyroid therapy, the basal metabolism and pulse increased, and there was some loss in weight. It is interesting to note that the metabolic rate remained high six months after discharge from the hospital. The parallelism between changing pulse and metabolic rate should be noted. Harris and Benedict: Carnegie Inst. Washington, pub. 279, 1919. Pirquet, C.: Pulsfrequenz u Sitzhöhe, Ztschr. f. Kinderh. **38**: 301, 1924. Read, J. M.: Correlation of Basal Metabolic Rate with Pulse Rate, J. A. M. A. **78**: 1887 (June) 1922. Schick, B., and Cohen, P.: Lowered Basal Metabolism in Postinfectious Stages and in Diseases Characterized by Slow Pulse, Am. J. Dis. Child. **30**: 291 (Sept.) 1925.

TABLE 8.—*Effects of Thyroid Therapy in Case 8* *

S. K., a boy, aged 9: surface area, 0.95 sq. m.; sitting height, 68 cm.; height, 124 cm.; diagnosis, hypothyroidism, convalescing from acute rheumatic fever; diet, 1,500 calories, 13 per cent protein.

Date, 1927	Weight, Kg.	Pulse	Total Calories	Comment
March 8	26	60	744	Symptom-free since March 3
9	26	58	744	
11	26	58	744	
14	25.8	56	756	Thyroid, 1½ grains daily
15	25.7	64	847	Thyroid, 3 grains daily
16	25	74	861	Thyroid, 4½ grains daily
18	25	76	1,005	Thyroid, 6 grains daily
20	24.8	80	1,008	
21	24.8	80	1,059	Discharged
April 30	....	80	1,106	In dispensary

Standards of Metabolism		Deviation on Admission	On Discharge
Pirquet	925 calories	Minus 20 per cent	Plus 14 per cent
Weight	1,020	Minus 27 per cent	Plus 3 per cent
Surface area	980	Minus 24 per cent	Plus 8 per cent
Height alone	980	Minus 24 per cent	Plus 8 per cent

* The basal metabolic rate was originally low, and the child had hair, skin, mental sluggishness and moderate obesity of hypothyroidism. Under thyroid therapy in moderate doses, the basal metabolism was raised to a more normal level, the pulse rate increased, the weight decreased, and there was a brighter mental reaction. It is interesting to note that the level of the basal metabolism remained high one month after discharge.

TABLE 9.—*Effects of Thyroid Therapy in Case 1 (Dispensary)* *

G. L., a girl, aged 10: surface area, 1.5 sq. m.; sitting height, 74 cm.; height, 145 cm.; diagnosis, obesity; diet, uncontrolled.

Date, 1927	Weight, Kg.	Sitting Height, Cm.	Height, Cm.	Pulse	Total Calories	Comment
May 4	57	74	145	80	1,248	Thyroid, ¾ grain (0.048 Gm.) daily
June 4	56	77	148	92	1,240	
11	56	79	150	92	1,300	
18	56.5	79	150	92	1,380	Thyroid, 1½ grains daily
25	56.5	80	151	90	1,382	Thyroid, 3 grains daily
July 1	56.5	80	152	96	1,346	Thyroid, 6 grains daily
15	57	80	152	96	1,368	Thyroid, 10 grains (0.65 Gm.) daily
22	57	82	154	96	1,312	Thyroid, 12 grains daily
29	57	82	154	96	1,300	Stopped thyroid

Standards of Metabolism		Deviation from Standard
Pirquet	1,095 calories for sitting height of 74 cm.	Plus 14 per cent
	1,344 calories for sitting height of 82 cm.	None
Weight	1,350	Minus 8 per cent
Surface area	1,300	None
Height	No figures available	None

* The increase in height should be noted. Basal metabolism remained relatively normal for changing height.

TABLE 10.—*Effects of Thyroid Therapy in Case 2 (Dispensary)* *

M. T., a girl, aged 11: surface area, 1.55 sq. m.; sitting height, 73 cm.; height, 144 cm.; diagnosis, obesity; diet, uncontrolled.

Date, 1927	Weight, Kg.	Sitting Height, Cm.	Height, Cm.	Pulse	Total Calories	Comment
March 16	60	73	144	100	1,120	Thyroid, ¾ grain daily
23	60	73	144	100		
April 4	60.5	73	144	100	1,113	Thyroid, 1½ grains daily
18	60	73	145	100		
May 1	59	73	145	96	1,070	Thyroid, 3 grains daily
15	58	74	146	96	1,048	
June 3	58	74	146	96	.....	Thyroid, 4 grains (0.26 Gm.) daily
17	58	75	148	96	1,096	Thyroid, 6 grains daily
30	57.5	75	148	96	.....	Thyroid, 9 grains daily
July 16	58.5	77	150	96	1,200	Stopped thyroid

Standards of Metabolism		Deviation from Standard
Pirquet	1,065 calories for sitting height of 73 cm.	Plus 5 per cent
	1,185 calories for sitting height of 77 cm.	None
Weight	1,350	Minus 17 per cent
Surface area	1,300	Minus 13 per cent
Height	No figures available	

* No real increase was present in basal metabolic rate which remained normal for changing height. Increase in growth should be noted. There were no signs of puberty.

TABLE 11.—*Effects of Thyroid Therapy in Case 3 (Dispensary)* *

H. Z., a girl, aged 12: surface area, 1.85 sq. m.; sitting height, 86 cm.; height, 159 cm.; diagnosis, obesity; diet, uncontrolled.

Date, 1926	Weight, Kg.	Pulse	Total Calories	Comment
Dec. 13	80	88	1,812	
27	..	..	1,800	
1927				
Jan. 29	80	90	1,745	Thyroid, 1½ grains daily
Feb. 19	78	88	1,738	Thyroid, 3 grains daily
March 5	78	88	1,712	Thyroid, 6 grains daily
12	78	84		
19	78	84	1,689	Thyroid, 9 grains daily
26*	77	84	1,735	Thyroid, 12 grains daily
April 2	77	80	1,730	Stopped thyroid

Standards of Metabolism		Deviation from Standard
Pirquet	1,500 calories	Plus 15 per cent
Weight	1,500	Plus 15 per cent
Surface area	1,500	Plus 15 per cent
Height alone	No figures available	

* Thyroid therapy had no effect on basal metabolism. The child reported the onset of menstruation two days before this visit. The question arises: Did the thyroid hasten puberty in this case?

TABLE 12.—*Effects of Thyroid Therapy in Case 4 (Dispensary)* *

G. M., a girl, aged 12: surface area, 1.05 sq. m.; sitting height, 72 cm.; height, 130 cm.; diagnosis, underheight; diet, uncontrolled.

Date, 1926	Weight, Kg.	Sitting Height, Cm.	Height, Cm.	Pulse	Total Calories	Comment
Oct. 23	33	72	130	88	1,000	Thyroid, 1½ grains
29	....	..	...	84	1,089	Thyroid, 3 grains
Nov. 10	33.5	..	...	76		
26	32.5	73	132	84		
Dec. 28	32.5	73	133	84	.....	Thyroid, 5 grains (0.32 Gm.)
1927						
Jan. 24	33	73	134	88	1,195	
Feb. 21	32.5	73	135	84	1,200	
March 16	33.5	73	135	70	1,228	Thyroid, 1 grain
April 30	34	73	136	76	1,184	
May 24	34	73	136	80		
July 15	35	75	138	80	1,150	Stopped thyroid

Standards of Metabolism		Deviation from Standard
Pirquet	1,036 calories	None
Weight	760	Plus 30 per cent
Surface area	1,000	None
Height alone	995	Plus 3 per cent

* Basal metabolism remained relatively unchanged. The increase in height should be noted. There were no signs of puberty.

TABLE 13.—*Effects of Thyroid Therapy in Case 5 (Dispensary)* *

F. E., a boy, aged 15: surface area, 1.8 sq. m.; sitting height, 82 cm.; height, 159 cm.; diagnosis, obesity, hypothyroidism; diet, uncontrolled.

Date, 1926	Weight, Kg.	Pulse	Total Calories	Comment
June 25	76.8	66	1,076	Thyroid, 2½ grains (0.16 Gm.) daily
July 7	74.5	80	1,200	Thyroid, 4 grains daily
10	73.5	80	1,272	Thyroid, 6 grains daily
23	73	100	1,272	
Aug. 9	72	100	1,300	Referred to adult clinic

Standards of Metabolism		Deviation from Standard
Pirquet	1,344 calories	Minus 13 per cent
Weight	1,800	Minus 35 per cent
Surface area	1,650	Minus 30 per cent
Height alone	No figures available	

* Note the increased pulse rate and basal metabolism in a boy who had the clinical manifestations of hypothyroidism corroborated by a low metabolic rate.

TABLE 14.—*Effects of Thyroid Therapy in Case 6 (Dispensary)* *

M. R., a girl, aged 11: surface area, 1.45 sq. m.; sitting height, 69 cm.; height, 137 cm.; diagnosis, obesity; diet, uncontrolled.

Date, 1927	Weight, Kg.	Sitting Height, Cm.	Height, Cm.	Pulse	Total Calories	Comment
March 22	58.2	69	137	66	1,490	Thyroid, 1 grain daily
April 7	58.2	69	137	66	.....	Thyroid, 1½ grains daily
May 8	57.6	71	138	66	1,492	Thyroid, 3 grains daily
June 3	57.5	72	140	66	.....	Thyroid, 4 grains daily
10	58	72	141	66	.....	Thyroid, 6 grains daily
17	58	72	142	66	1,389	Thyroid, 9 grains daily
July 9	57	73	144	66	1,300	Thyroid stopped

Standards of Metabolism		Deviation from Standard
Pirquet	980 calories for sitting height of 69 cm.	Plus 35 per cent
	1,066 calories for sitting height of 73 cm.	Plus 23 per cent
Weight	1,350	None
Surface area	1,300	None
Height	1,037	Plus 25 per cent

* The increase in growth with slight loss of weight should be noted. Basal metabolism diminished somewhat; pulse unaffected.

COMMENT

In our series of eight patients seen in the hospital, five had a normal basal metabolism, one had a high basal metabolism often found in overnourished, obese children,[5] and two, who were suspected of having a subnormal thyroid gland, had low basal metabolism rates. In the patients with a normal or high basal rate, thyroid therapy did not affect the basal metabolism, nor were there any signs of physiologic reaction to thyroid; i.e., increased pulse rate, loss of weight, increased diuresis, tremor, etc. In case 1, the basal metabolism rose at times, due to a complicating infection with fever.[6] In case 5, the basal metabolism actually decreased, but this may have been due to a partial inanition which this child was undergoing, and which was noted even before thyroid therapy was started. It is well known that inanition lowers the basal metabolism.[7] In case 6, when 12 grains of thyroid extract and 5 mg. of thyroxin were given on the same day, there was a transient increase of basal metabolism for two days. The pulse rate rose, diuresis increased, and the boy was tremulous and complained of dizziness. This was the only time we were able visibly to affect a child with an initially normal basal metabolism by thyroid therapy.

The two patients with hypothyroidism showed a lowered basal metabolism at the outset. Thyroid substance in doses of from 6 to 9 grains daily quickly brought the basal metabolic rate to a point above normal. Contemporaneously, the weight decreased; urine was excreted in larger amounts; the pulse rate rose, and soon a quicker and sharper mental reaction was noticeable. It was interesting to note that in these two cases oral therapy alone and in fairly small doses was efficacious, while far larger doses did not affect the basal metabolism of the six normal children.

In our series of six patients seen in the dispensary, where our follow-up studies were longer, we encountered four with a normal basal metabolism, and two who had an endocrine imbalance with a subnormal basal metabolism. As in our series seen in the hospital, as much as 12 grains daily of thyroid substance over a fairly long period did not affect the basal metabolism of the four normal children; but in the two subnormal cases, the basal metabolism was brought to a normal level with smaller doses. In these two cases, the pulse rate increased, the weight decreased, and the children showed a better nervous response.

In the four normal children, while the basal metabolism remained unaffected, there was an extraordinary increase of growth in a rela-

5. Grafe: Ergebn. d. Physiol., 1923, vol. 21.

6. DuBois, E. F.: Metabolism in Fever, J. A. M. A. **77**:352 (June 30) 1921.

7. Benedict, F. G.: Influence of Inanition on Metabolism, pub. 77, Carnegie Inst., Washington, 1907.

tively short time during the period of thyroid therapy. The normal increase between the ages of 10 and 12 is about 2 inches (5 cm.) yearly, the greater part of which occurs in the late summer and early autumn.[8] In our cases, there was an increase of from 6 to 9 cm. in a few months, and out of season. This was so striking that it excited independent comment. The weight in these cases either remained stationary or actually decreased, thus excluding the effects of the natural growth of increasing age.

The effect of thyroid therapy on persons with a subnormal thyroid has been studied and recognized for many years. The prompt response to small or moderate doses in such cases causes our results in similar cases not to be surprising. Children with a subnormal thyroid respond to thyroid therapy, just as adults with a subnormal thyroid do. Plummer and Boothby[9] even went so far as to demonstrate a mathematical ratio between the dosage of thyroxin and the consequent increase in basal metabolism in myxedematous cases.

However, the lack of response to thyroid therapy in our normal children created some surprise. Our surprise was increased when we observed the tremendous stimulative effect that thyroid seemed to have on their growth processes, while their basal metabolic rates remained practically unchanged. We concluded that there must be a difference in the action of the thyroid on normal persons before and after puberty.

Studies in experimental thyroid therapy throw much light on the question of the effect of thyroid substance on normal persons and on animals. Magnus-Levy,[10] Asher,[11] Krehl,[12] Gregor,[13] Becker,[14] Arnoldi and Leschke,[15] Thannhauser and Eppinger[16] and Biedl[17] did not find an increase in basal metabolism in normal persons after thyroid therapy.

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8. Gebhart, John A.: How Children Ought to Grow, Child Health Library, vol. 8.

9. Plummer, H., and Boothby, W. M.: Specific Dynamic Action of Thyroxin, Am. J. Physiol. **55**:295, 1921.

10. Magnus-Levy, in von Noorden: Handbuch d. Path. d. Stoffwechsels, ed. 2, Berlin, Hirschwald, 1907, p. 323.

11. Asher, L.: Die Wirkung des Schilddrüsenhormons, Therap. Halbmonatshefte, 1920, vol. 34.

12. Krehl: Pathologische Physiologie, ed. 10, Leipzig, Vogel, 1920, p. 136.

13. Gregor, K.: Ueber die Unschädlichkeit der Verfütterung grosser mengen von Thyroidea in Kinder, Monatschr. f. Kinderh. **1**:318, 1903.

14. Becker: Beitrage zur Thyroidinwirkung, Deutsche med. Wchnschr. **21**: 600, 1895.

15. Arnoldi and Leschke: Die Wirkung des aus Endokrinen Drüsen hergestellten Präparate auf den Gaswechsel, Ztschr. f. klin. Med. **92**:364, 1921.

16. Thannhauser and Eppinger: Verhandl. d. 34 Deutsch. Kongr. f. inn. Med., Wiesbaden, 1922.

17. Biedl, A.: Verhandl. d. 34 Deutsch. Kongr. f. inn. Med., Wiesbaden, 1922.

Gabbe [18] and Fujimaki and Hildebrandt,[19] working with rats, and Sierens and Noyons,[20] experimenting with pigeons, found that thyroid caused an increase in basal metabolism. Bowen and Boothby,[21] Plummer and Boothby,[9] Aub and Stern,[22] Kowitz,[23] Thiele and Nehring [24] and Löhr,[25] working with normal adults, reported that thyroid increases the basal metabolism. These opposing views are perhaps reconcilable, if we bear in mind that normal adults may have an individual reaction to thyroid, so that while some may respond others apparently remain unaffected. Krehl [12] and Asher,[11] who opposed the view that thyroid affects the normal person, admit the individuality of response. The authors have also noted that some adults they observed responded to thyroid therapy, while others apparently did not. Carlson, Rooks and McKie [26] found that the same holds true of animals, some groups of which are more resistant to the effects of thyroid therapy than others. This individuality of response may be an index of thyroid activity in the person; the more active the gland, the less marked the effect of ingested thyroid, an opinion supported by Kendall.[27] Thus, in the cretin or the myxedematous patient, in whom the gland is inactive, the response to small or moderate doses of thyroid substance is prompt; while in normal persons large doses are needed, and even then the effect cannot be predicted.

Studies on normal children have been meager. Becker [14] was the first to study the effects of thyroid on a normal child who swallowed ninety 0.3 Gm. tablets of a potent thyroid extract without any observed

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18. Gabbe: Kongr. f. inn. Med., 1925, p. 186.

19. Fujimaki, Y., and Hildebrandt, F.: Ueber die Wirkung des Thyroxins auf den Stoffwechsel (nach Versuchen an Ratten), Arch. f. exper. Path. u. Pharmakol. **96**:292, 1923.

20. Sierens, A., and Noyons, A. K.: L'influence de la thyroxine sur le metabolisme du pigeon, Compt. rend. Soc. de biol. **94**:789, 1926.

21. Bowen and Boothby: A Study of the Effect of Thyroid Substance on Basal Metabolism, J. Urol. **1**:469, 1917.

22. Aub, J. C., and Stern, N. S.: Influence of Large Doses of Thyroid Extract on Total Metabolism, Arch. Int. Med. **21**:136 (Jan.) 1918.

23. Kowitz, H. L.: Experimentelle Untersuchungen zu den Problem der Schilddrüsenfunktion, Ztschr. f. d. ges. exper. Med., 1923, vol. 34; Die Funktion der Schilddrüse und die Methoden ihrer prüfung, Ergebn. d. inn. med. u. Kinderh., 1925, vol. 27.

24. Thiele, J., and Nehring, A.: Untersuchungen des respiratorischen Gaswechsels unter dem einflusse von Thyroideapräparaten, Ztschr. f. klin. Med., 1896, vol. 30.

25. Löhr, H.: Ueber der Wirkung des Thyroxins auf den Menschlichen Organismus, Ztschr. f. d. ges. exper. Med. **46**:429, 1925.

26. Carlson, A. J.; Rooks, R., and McKie, J. F.: Attempts to Produce Experimental Hyperthyroidism in Mammals and Birds, Am. J. Physiol. **30**:129, 1912.

27. Kendall: Endocrinology **3**:156, 1919.

effect. Fleming [28] gave large amounts of an active thyroid extract to mongolian idiots over a relatively long time without apparent effect or increase of basal metabolism. Gregor [13] fed large amounts of fresh gland for many days to three idiotic children, one a mongol, without any effect on pulse rate, respiration, blood pressure, appetite, urinary excretion or weight. Bass [29] told of a child who swallowed the contents of a nearly full bottle of thyroid tablets without any apparent effect. Our series of cases is the largest reported in children [30] and, like Fleming, we did not observe any effect on the basal metabolism in our normal patients.

Thyroid extracts have not only a metabolic action, but a morphogenetic effect, which is naturally best observed in young animals. This is most clearly seen in the delayed growth and subnormal mentality of cretins, and in the cessation or retardation of growth seen in thyroidectomized animals. Gudernatsch [31] was able to accelerate the growth of the tadpole by feeding it thyroid, converting it into a frog, withal a small one, in a few days. His experiments have been corroborated by Uhlenhuth,[32] Morse,[33] Abderhalden,[34] Allen,[35] Swingle [36] and Hoskins.[37] Similar results in acceleration of growth were obtained with salamanders.[38] Growth can be accelerated in animals which do not even possess a thyroid gland by feeding thyroid, as in the larvae of the

28. Fleming, G. B.: The Respiratory Exchange in Cretinism and Mongolian Idiocy, Quart. J. Med. **16**:11, 1922.

29. Bass, Murray H.: Personal communication to Dr. Topper.

30. A series of twenty mongolian idiots has been under observation at the Massachusetts General Hospital over a period of four years. Most of these showed definite mental and physical improvement under thyroid therapy. The data is as yet unpublished.

31. Gudernatsch, J. F.: Feeding Experiments on Thyroidectomized Tadpoles, Am. J. Anat., 1914, vol. 15; Anat. Rec., 1917, vol. 21. Goldberg, S. A.: Changes in Organs of Thyroidectomized Sheep and Goats, Quart. J. Exper. Physiol., 1927, vol. 17. Biedl, A.: Innere Sekretion, ed. 4, Berlin and Vienna, 1922.

32. Uhlenhuth, E. J.: Relation Between Thyroid Gland, Metamorphosis and Growth, J. Gen. Physiol. **1**:473, 1919.

33. Morse, W.: Biol. Bull. **34**:149, 1918.

34. Abderhalden: Relation Between Thyroid Gland Substance and Growth, J. Exper. Physiol., 1919.

35. Allen, B. M.: Results of Thyroid Removal, J. Exper. Zool., vol. 24, no. 3, January, 1918.

36. Swingle, W. W.: The Acceleration of Metamorphosis in Frog Larvae by Thyroid Feeding, J. Exper. Zool., 1918, vol. 24. Swingle, Helff and Zwemer: The Effect of Thyroxin on Amphibians and Mammals, Am. J. Physiol. **70**:208, 1924.

37. Hoskins, E. R., and Hoskins, M. H.: Growth and Development of Amphibia as Affected by Thyroidectomy, J. Exper. Zool., 1919, vol. 25.

38. Uhlenhuth, E. J.: Effect of Iodine and Iodothyrine on Larvae of Salamanders, Biol. Bull. 42, no. 3, March, 1922.

flesh fly (Zavrel and Kunkel [39]). The rate of division of protozoa can be markedly increased by the addition of thyroid substance to the culture medium (Shumway and Novikoff.[40] Carrell [41] observed that thyroid extract causes the growth of brain tissue and other tissues to increase several times as rapidly as in the absence of thyroid substance. This is in accord with the slower regeneration of tissue noted in thyroidectomized animals. Bircher [42] found that feeding of thyroid caused increased and early calcification of bones in mammals, while Bircher, Hofmeister and von Eiselsberg [42] found that the extirpation of the thyroid resulted in a remarkable retardation of the process of ossification of both the epiphyses and the synchondroses. These observations bear out Kendall's [43] opinion that thyroxin, the active thyroid principle, is merely a catalytic agent for metabolic processes, increasing metabolism in the direction in which it is progressing. In other words, thyroid affects metabolism quantitatively, not qualitatively.

The basal metabolic rate is an accurate index of the metabolic activity of the resting animal, and the thyroid gland is intimately related to the basal metabolic rate. But the thyroid gland is concerned with more than the basal metabolism. It seems to control, or partly control, the specific dynamic action of foods.[44] In hyperthyroidism, the specific dynamic energy of foods is increased, as is the cost of work, suggesting that exercise affects metabolism to some extent through the thyroid gland. Nitrogen metabolism, particularly the deposit protein, is markedly affected by thyroid.[21] Paradoxically, it seems, nitrogen is retained by the cretin, but is lost by the normal adult through thyroid therapy. We will return to this point later. Water and salt metab-

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39. Zavrel, J.: Influence of the Thyroid Gland on Growth of Chironomid Larvae, Compt. rend. Soc. de biol. **96**:1096, 1927. Kunkel, B. W.: The Effects of the Ductless Glands on Development of Flesh Flies, J. Exper. Zool. **26**:255, 1918.

40. Shumway, W.: Effects of Thyroid upon Paramecium, J. Exper. Zool. **22**:529, 1917; Effects of Thyroid on Division Rate of Paramecium, ibid. **17**:314, 1914. Novikoff, M.: Ueber die Wirkung des Schilddrüsenextraktes auf Ciliaten, Arch. f. Protistenk. **11**:309.

41. Carrell, A.: Artificial Activation of Growth in Vitro of Connective Tissue, J. Exper. Med. **17**:149, 1913.

42. Bircher, E.: Zur Wirkung der Thyroidintabletten auf das normale Knochenwachstum, Arch. f. klin. Chir. **91**:554, 1910. Hofmeister: Ueber Störungen die Knochenwachstums by Cretinismus, Fortschr. a. d. Geb. d. Röntgenstrahlen 1. Untersuchungen über die Folgen des Schilddrüsenverlustes, Beitr. z. klin. Chir., 1894, vol. 11. Von Eiselsberg: Wachstumssstörungen bei Tieren nach frühzeitiger Schilddrüsenextirpation, Arch. f. klin. Chir., 1895, vol. 49.

43. Kendall: The Chandler Lecture, 1925, Columbia University Press **36**:80, 1925.

44. Magnus-Levy: Ztschr. f. klin. Med. **33**:269, 1897. Pribram and Porges: Wien. klin. Wchnschr. **21**:1584, 1908. Undeutsch: Inaug. Diss., Leipzieg, 1913.

olism[45] and hence, blood volume, are also regulated by the thyroid gland. In fact, Eppinger,[2] who denies that thyroid affects the basal metabolism of the normal person, is an enthusiastic advocate of the positive effects of thyroid on water and salt metabolism. The action of thyroid on the nervous system, especially the autonomic system,[46] is well known. The rôle of the thyroid gland in growth and regenerative processes has already been discussed.

All these facts raise the question whether the basal metabolic rate should be the only criterion of the efficacy of thyroid therapy in normal persons, since the thyroid gland is concerned with so many other metabolic processes. Is it not conceivable that the basal metabolism may remain unaffected in children, while other metabolic processes are influenced by thyroid therapy?

The theory that we have evolved to explain the difference between thyroid action in the normal adult and in the normal child is that thyroid, a metabolic catalyst, increases the phase of metabolism which is dominant in the individual: anabolic, or growth processes, in the child, and catabolic, or oxidative processes, in the adult. This is in line with Kendall's opinion that thyroxin speeds metabolism in the direction in which it is going. In his monograph on the internal secretory glands, Biedl,[31] thus sums up the results of his experiments with animals. He says that there is a certain amount of difference between the signs of thyroid suppression in young growing animals and in adult animals. In the young, the derangement of metabolism is manifested with peculiar distinctness in the changes which take place in the processes of growth; the changes in the older animals are principally confined to changes in metabolic processes, the clinical manifestation of which are loss of appetite, sluggish digestion and emaciation, finally resulting in cachexia thyreopriva and death. Our theory explains Biedl's results. Thus, thyroid affects the growth processes of the normal child, while the basal metabolism remains unchanged; whereas in the adult, whose growth processes are complete, the basal metabolism is increased in the persons whose catabolisms are such as to allow further increase. This theory fits in with the paradoxic fact that the cretin under thyroid therapy retains nitrogen, while the normal adult under the same therapy loses nitrogen. This theory also serves to explain the increased tolerance of children for iodides which exert their metabolic influence through

45. Falta et al.: Ueber Beziehungen der inneren Medizin zum Salzstoffwechsel **26**:138, 1909. Soderstrom and DuBois: Clinical Calorimetry, Arch. Int. Med. **19**:823 (May) 1917. Veil, W. H., and Bohn, H.: Der Obachtungen des Wassers und Salzwechsels bei Thyroidinextraktbehandlung, Deutsches Arch. f. klin. Med. **139**:212, 1922.

46. Grafe, E.: Ergebn. d. Physiol., 1923, vol. 21.

the thyroid gland.[47] It explains why exopthalmic goiter induced by iodide therapy is rare and practically unheard of in a child, while in the adult it is not a rare phenomenon.

SUMMARY AND CONCLUSIONS

1. The effect of thyroid therapy on children was studied in eight patients in the wards and in six in the dispensary.

2. In four children with subnormal thyroid activity, as evidenced by a subnormal basal metabolism and clinical manifestations of hypothyroidism, thyroid in small or moderate doses promptly brought the basal metabolic rate to a normal level, where it stayed even after thyroid therapy was discontinued.

3. In one child with a normal metabolism, 12 grains of thyroid extract by mouth combined with 5 mg. of thyroxin caused a transient increase in pulse rate and basal metabolic rate. Here the combined dosage was so large that it was beyond clinical value.

4. In nine children with a normal basal metabolic rate, as much as 15 grains of thyroid extract daily did not increase the basal metabolism. Four of these children, whose measurements were followed carefully, showed a remarkable increase in growth during this period.

5. Since thyroid extract in relatively large doses does not seem to have any effect on the basal metabolism of normal children, the stimulative effect on their growth leads us to question whether the basal metabolism should be the criterion of the effect of thyroid therapy in normal children, especially as thyroid produces other physiologic and metabolic responses.

6. Since the action of thyroid on normal children seems to be different from the action of thyroid on normal adults, we offer a theory to explain this difference and hope thus to stimulate further investigation.

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47. Marine, D., and Williams, W. H.: Relation of Iodine to Thyroid Gland, Arch. Int. Med. **1**:350 (May) 1908. Hunt, R.: The Relation of Iodine to the Thyroid Gland, J. A. M. A. **49**:1323 (Oct. 19) 1907.

ANTENATAL INFECTION A FACTOR IN FETAL MORBIDITY *

EMILE DUSKES, M.D. †
AND
EVA F. DODGE, M.D.
BALTIMORE

The obstetrician and the general practitioner are constantly confronted with the experience of delivering children who are either dead at birth or so diseased or injured that death occurs in a few hours or days. The most usual causes are syphilis, toxemia, disease or malpresentation of the placenta, particularly placenta praevia, operative delivery because of contracted pelvis, excessive size of child and malpresentation or prolonged delivery from any cause. The literature also contains many references to a relatively small group of infections, such as typhoid, scarlet fever, malaria, smallpox, measles, tuberculosis and anthrax (Williams [1]). We wish to add to the already reported cases of antenatal infection two cases recently examined.

REPORT OF CASES

CASE 1.—L. H., a colored woman, a quintipara, aged 26, whose family history was negative, had had sore throat occasionally over a period of many years. A normal menstrual history showed that her previous pregnancies had ended at full term and spontaneously; all children were living and healthy. The last menstrual period began on Oct. 26, 1926, and pregnancy was progressing normally. Urinalysis was normal, but the Wassermann reaction was four plus. With the exception of carious teeth, the results of physical examination were negative. On May 2, 1927, at 5:30 p. m., while at work at her home, she gave spontaneous birth to a slightly macerated, moderately well developed, dead female child, 43 cm. in length. The puerperium was uneventful. A postmortem examination of the fetus was made. All the intestinal loops, the generative tract and the urinary bladder were firmly adherent to one another and covered with a somewhat greenish, flaky exudate. Cultures were taken. An attempt to separate any of the coils would result in the tearing of the bowels. The stomach was not involved. The liver was of normal size and adherent at its margin, but the remaining surface was smooth and the organ itself soft. The spleen was enlarged, measuring 5.5 by 3.2 by 1.9 cm. The other abdominal and thoracic organs did not show any special gross deviations. There was not any general glandular enlargement; in the long bones, the epiphysodiaphysial line was irregularly defined, thickened

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* From the Departments of Pathology and Obstetrics of the University of Maryland School of Medicine.

† Deceased.

1. Williams, J. W.: Textbook of Obstetrics, ed. 4, rev., New York, D. Appleton & Company, 1921.

and of a reddish-white appearance. The bacteriologic examination showed pneumococci and gram-negative bacilli in the smears and in culture. Microscopic sections of all of the organs showed typical syphilitic changes, and the adherent intestinal loops showed a recent fibrinous reaction. Levaditi stain showed innumerable spirochetes in the spleen and MacCallum's special bacterial stain demonstrated definite gram-positive diplococci in the peritoneal adhesions.

On inquiry, the information was obtained that a week before delivery the patient had had a sore throat which had cleared up in a few days. She had not experienced chills, fever, pains in the joints or cough. On May 12, 1927, cultures were taken from the blood, nose and throat. The first was negative; from the second, hemolytic *Staphylococcus albus,* streptococcus and a few pneumococci were obtained. The throat cultures showed streptococci, *Staphylococcus aureus* and hemolytic *Staphylococcus albus.*

In this case there is what appears to be a superimposition of one disease on another. The fetus was definitely syphilitic; in addition, pneumococci were demonstrated in direct smears from the peritoneum, grown on culture and shown in the fixed tissue. To prove that the mother's sore throat was caused primarily by a pneumococcic infection is impossible as pneumococci are harbored in the upper respiratory tract in a large number of persons. The following appears to be a plausible explanation. It is conceivable that the illness was caused by the usual staphylococci and streptococci but that in the process of lowered resistance the pneumococci gained entrance to the blood stream and to the fetus, and manifested itself as an additional reaction to an already diseased state.

Case 2.—A colored woman, M. H., a tertipara, aged 32, sent in an emergency call to the obstetric service on April 17, 1927, saying that three and a half hours previously she had delivered herself of a premature child. Bleeding continued and, at the end of an hour, it was thought best to remove the placenta manually. The patient was given an anesthetic and cleaned; then an episiotomy was performed because of a small vaginal outlet. The placenta was quite adherent, and was removed with considerable difficulty. The episiotomy was repaired, and the condition of the patient following return to consciousness was fair. She was placed in Fowler's position; an ice-bag was put to the abdomen, ergot was given and fluids were forced. The following day the temperature was 101.6 F. and the pulse rate was 130. On the second day, the patient was comatose, with the temperature at 97 and the pulse rate 140. The abdomen was tender and slightly distended. The patient died at 3:15 p. m. the same day.

Autopsy was performed at 9:15 that evening, and the anatomic diagnosis was: acute putrid endometritis, thrombosis of right ovarian vein, cloudy swelling of heart and liver, acute congestion of kidneys, edema of lungs, acute splenic tumor, early arteriosclerosis of the aorta and fibrous peritoneal adhesions of the right upper quadrant. A blood culture taken at autopsy showed pneumococci. The fetus was a male in good preservation, measuring 33 cm. in length. A careful complete gross and microscopic examination did not reveal any changes. Blood culture showed pneumococci. Spirochetes or other microorganisms were not demonstrated in the tissues.

Unfortunately, the history in this case is not complete or entirely reliable. There was a suspicion that abortive interference had taken place, but there is no doubt that a septicemia had occurred. The same organism was cultured from the blood of the fetus and of the mother, indicating definitely a maternal transmission.

In the majority of cases of maternal infections, the placenta acts as a strong barrier inhibiting the introduction of destructive agents from the maternal blood and lymph. At times this barrier is weakened and penetrated, but the fact that the healthy infant is bacteriologically sterile at the moment of birth is conclusive evidence that the placental barrier is effective. However, by means of the placenta, infective agents may reach the fetus. Disease in the fetal period is comparable to postnatal disease with the modifying factors of the nature of the fetal environment and the influence of the placental circulation (Schumann [2]).

For intra-uterine bacterial transmission, it is not necessary that there should be any rupture either in the maternal or the fetal placental vessels (Ausset [3]). Placental bacteremia may take place through any of three routes (Slemons [4]): (1) the organisms may pass from the maternal circulation across the decidua, the chorion and the amnion; (2) the bacteria may travel through the peritoneal cavity down the fallopian tubes, or (3) the agents may ascend from the vagina through the cervical canal. The first method of fetal infection when labor has not commenced or when the fetal membranes have not been ruptured is of principal interest.

The results of fetal infection are apparent at birth in various ways. The child may be born dead, moribund, sickly or apparently healthy and no signs or symptoms will appear until a few days later, when the newborn child rapidly succumbs. At autopsy pathologic changes are seen, which by the nature of the reaction present are evidently older or of longer duration than the conditions of the neonatal life would indicate.

Of these different types many instances have been recorded, and the following representative examples have been collected. We shall not review fetal endocarditis or discuss the possible fetal inflammatory origin of Jackson's membrane or the different bands of Arbuthnot Lane.

REVIEW OF THE LITERATURE

Ballantyne [5] mentioned two patients who died of peritonitis a few days after birth. Grosse and LeLorier [6] reported that a child was born apparently healthy, but two days after birth gastro-intestinal disturbances

2. Schumann, E. A.: Some General Observations on Antenatal Pathology, Am. J. Obst. & Gynec. **75**:953 (June) 1917.

3. Ausset, E.: Des infections intra-utérines du foetus (excepté la syphilis), Bull. méd. du nord, Lille **35**:401, 497 and 581, 1896.

4. Slemons, J. M.: Placental Bacteraemia, J. A. M. A. **65**:1265 (Oct. 9) 1915

5. Ballantyne, J. W.: Studies in Foetal Pathology and Teratology, Tr. of the Edinburgh Obstet. Soc. **17**:53, 1891-1892.

6. Grosse, A., and LeLorier, V.: Péritonite datant de la vie intrautérine chez un nouveau-né, Compt. rend. Soc. d. obst. de gynéc et de pédiat. de Paris **7**:8, 1905.

appeared, and on the fourth day an adherent peritonitis was found. Westphal [7] encountered a healthy primipara, aged 24, who gave spontaneous birth to a full term fetus that lived only twenty-four hours. Abdominal exploration revealed adherent peritonitis without any evidence of syphilis or any micro-organisms.

In his inaugural dissertation, Spies [8] reported a case of fetal peritonitis occurring in a healthy secundipara who six weeks prior to the time of the birth of her child had had an attack of tonsillitis followed by an endocarditis. He collected two other cases of intra-uterine death in which chronic peritonitis was present and six similar ones in which the infant lived from twelve to forty-seven hours.

Warwick [9] observed a case of a full-term infant that lived only two and a half hours. At necropsy it presented typical bronchopneumonia, and smears from the lungs showed polymorphonuclear leukocytes and gram-positive cocci in pairs and chains. The mother appeared to be entirely normal. In another case of bronchopneumonia, he found that the infant lived three days. At the time of the delivery, the mother suffered from a severe attack of tonsillitis.

Browne [10] recorded a case in which a sickly child lived eight hours. At postmortem examination there was a pleural effusion, and both lungs were solid with pneumonia in the stage of gray hepatization. In another case, in which a new-born child died on the third day it was found that the infant had had pneumonia, double empyema and septic endocarditis.

In 1877, Murillo [11] performed an autopsy on a child that had lived fifteen hours; he demonstrated a serofibrinous peritonitis.

Mauclaire and Alglave [12] delivered a child born with an elevated temperature. At birth, it started to vomit frequently a yellowish-green followed by a black material. Bowel movements did not occur for three days; purgatives were unsuccessful, and the child died on the sixth day. The abdominal cavity showed a generalized fibrinous and fibrous peritonitis, and the intestinal coils were tangled and matted together. A maternal uncle had died of tuberculosis. The personal history of the

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7. Westphal, U.: Kasuistischer Beitrag zur fötalen Peritonitis, Monatschr. f. Geburtsh. u. Gynäk. **66**:245, 1924.

8. Spies, P.: Ueber fötale Peritonitis, Inaugural Dissertation, Universität Heidelberg, 1917.

9. Warwick, M.: Necropsy Findings in New-Born Infants, Am. J. Dis. Child. **21**:488 (May) 1921.

10. Browne, F. J.: Neo-Natal Death, Brit. M. J. **2**:590 (Sept. 30) 1922.

11. Murillo, A.: Peritonitis jeneral en un feto que muere poco despues de nacer, Rev. méd. de Chile **6**:179, 1877.

12. Mauclaire and Alglave: Un cas de péritonite tuberculeuse ancienne, fibreuse, chez un nouveau-né âgé de 6 jours, Bull. et mém. Soc. anat. de Paris **74**:1057, 1899.

father and mother were both normal, but throughout the pregnancy the mother had had epileptiform seizures and edema of the lower extremities.

Faix and Herbinet [13] recorded a case of a child born prematurely at seven and a half months. Fever appeared on the preceding day, followed by jaundice, and on the third day the child succumbed. At autopsy, a fibrinous pleurisy was found on the right side, from which staphylococci were isolated.

Thore [14] and Silbermann [15] quoted instances of infants living only a few days because of pleural and peritoneal infections. In 1889, Netter [16] reported an unusual case of a woman, aged 33, who developed a typical lobar pneumonia during the eighth month of her pregnancy. Two days after the crisis, the child was born. It remained well for two days, but died on the fourth. Pneumococci were isolated from the blood, and a generalized meningitis and peritonitis was encountered. Levy [17] described a woman nine months parturient who shortly after the birth of a child died of pleuropneumonia. The baby succumbed three days later to a pericarditis and bronchopneumonia. Vinay [18] saw a woman, who, thirty-six hours before death caused by pneumonia, delivered a well developed although cyanosed fetus that expired on the third day as a result of a lobar pneumonia; the blood and pneumonic exudate showed pneumococci.

As early as 1832, Cruveilhier [19] brought the attention of the Anatomical Society of Paris to the frequency of peritoneal inflammations in the new-born. He cited the case of a child who died on the seventh day from acute peritonitis. On the ninth day of the puerperium, the mother succumbed to a fatal peritonitis. Of interest is a specimen in the museum of Guy's Hospital of a six months old fetus covered with smallpox pustules; the child was born when the mother was recovering from that disease (Madge [20]).

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13. Faix and Herbinet: Péritonite à staphylocoques chez un nouveau-né, Bull. de la Soc. d'obstet. de Paris, **8**:205, 1905.

14. Thore: De la péritonite chez les enfants nouveau-né, Arch. gén. de méd. de Paris **11**:389 (Août) 1846.

15. Silbermann, O.: Ueber Bauchfellentzündung Neugeborener, Jahrb. f. Kinderh., Leipzig **18**:420, 1882.

16. Netter: Transmission intra-utérine de la pneumonie et de l'infection pneumonique chez l'homme et dans l'espèce animale, Compt. rend. Soc. de biol. **41**:187, 1889.

17. Levy, quoted by Chambrelent: De l'influences des maladies du poumon de la mère sur l'état de santé du foetus, Rev. mens. de gynéc., d'obstét. et pédiat. **3**:146, 1901.

18. Vinay, quoted by Chambrelent (footnote 17).

19. Cruveilhier: Bull. Soc. anat. de Paris **7**:3, 1832.

20. Madge, H.: Diseases of the Foetus in Utero, London, Henry Renshaw, 1854.

Franklin [21] related a case of a vaccinated woman exposed to smallpox who remained well, but the fetus died of smallpox in utero.

Traugott [22] gave the details in a unique case of fetal diphtheria. A primipara, aged 22, pregnant four months, developed a sore throat and an elevated temperature; throat cultures showed diphtheria bacilli. On the second day after the onset of the complaints, the patient received antitoxin; in three days the temperature fell by lysis to normal, and the woman felt well. A culture from the throat was negative. However, five days later the patient's temperature rose again, and on the seventeenth day from the time of the initial symptoms the patient had a chill and respiratory disturbances. Examination of the heart and lungs did not reveal any changes. On the nineteenth day, there occurred a spontaneous delivery of a recently dead female fetus measuring 22 cm. in length. The puerperium was essentially uneventful, and eight months later, the woman was in the second half of another pregnancy. The peritoneal cavity of the fetus in this case, contained an excessive amount of fluid in which diphtheria bacilli were found. The liver was enlarged and on the surface were innumerable small pale yellowish-white stippled areas; microscopically, these contained masses of diptheria bacilli.

Oehler [23] observed a case of typical advanced abdominal tuberculosis in a new-born infant. Calmette, Valtis and Lacomme [24] described tuberculous infected fetuses delivered from tuberculous mothers. Curtis [25] isolated the streptococcus as the direct cause of abortion in several cases which he reported. Straus and Chamberland,[26] Regan, Litvak and Regan,[27] reported the finding of anthrax in the fetus transmitted from the mother.

Cornell [28] cited the instance of a parturient woman whose history was essentially normal. Pregnancy was uneventful with the birth of a female fetus in asphyxia pallida with all the serous cavities containing more than the normal amount of fluid. A pneumococcus and a gram-positive bacillus grew on cultures from the pericardium. Pneumococci and staphylococci were isolated from the pleural cavity. The Wassermann

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21. Franklin, quoted by DeLee.

22. Traugott, M.: Ueber fötale Diphtherie, Zentralbl. f. Gynäk. **50**:3255, 1926.

23. Oehler, quoted by Madge (footnote 20).

24. Calmette, A.: Valtis, J., and Lacomme, M.: Transmission intra-utérine du virus tuberculeux de la mère à l'enfant, Presse méd. **34**:1409, 1926.

25. Curtis, in Peterson, Haines and Webster: Legal Medicine and Toxicology, ed. 2, Philadelphia, W. B. Saunders Company, 1923, vol. 1, p. 979.

26. Straus, I., and Chamberland, C.: Passage de la bactéridie carbonnêuse de la mère au foetus, Compt. rend. des séances et mém. Soc. de biol. **4**:804, 1882.

27. Regan, J. C.; Litvak, A., and Regan, C.: Intra-uterine Transmission of Anthrax: Report of Case, J. A. M. A. **80**:1769 (June 16) 1923.

28. Cornell, E. L.: The Pneumococcus Found in a Case of Still-Birth, J. A. M. A. **68**:843 (March 17) 1917.

reaction in both mother and child was negative. Cultures taken from the tonsillar crypts and the vaginal discharge of the mother showed pneumococci and staphylococci. In his thesis, Lorain [29] reported finding ten fetuses dead of peritonitis; in three instances, the mothers died following puerperal fever.

Chambrelent [30] related the case of a woman who during the eighth month of her pregnancy developed typhoid fever. On the fifth day of the disease, a fetus was born. It gave a positive Widal reaction. Although severely ill, the child survived. By subcutaneous typhoid inoculations into the guinea-pig, Gory and Dalsace [31] were able to recover the organism from the fetus.

DeLee [32] cited some unusual cases which distinctly showed the influence of the maternal factor in diseases of the fetus in utero. In one case, a mother developed eclampsia during the seventh month; a rapid delivery was performed, and as the head was born, pure pus exudated from the nostrils, and cultures showed the presence of pneumococci. The mother made an afebrile recovery. In another case, a woman in the eighth month of her pregnancy experienced a slight pharyngitis which compelled her to remain in bed for a few days. On arising, fetal movements ceased. Delivery took place four weeks later, *Streptococcus viridans* being isolated from the heart, liver and spinal cord. In one pregnancy, a spontaneous premature delivery occurred followed by a prolonged septic puerperium. Up to the time of the pregnancy, the woman was in good health. At the seventh month, a macerated fetus was spontaneously delivered, and cultures showed a nonhemolytic streptococcus. The mother had a fever soon after the delivery; symptoms of cerebral thrombosis developed, and the patient died. A primipara had two attacks of abdominal pain ascribed to gallstones three weeks before labor at term. The fetus was born dead with a hemolytic pneumococcus cultured from the liver, heart, brain and spinal cord. In another case, a woman was at full term; at the end of the second stage of labor, the fetal heart became irregular and ceased to beat. Staphylococci were found in the blood and pneumococci and staphylococci in the pericardial and pleural cavities.

DeLee described the experience of Liddell and Tangye in an outbreak of scarlet fever in a small village. Four of five children developed scarlet

29. Lorain, P.: De la fièvre puerpérale chez la femme, le foetus et le nouveau-né, Thèse de Paris, 1855.

30. Chambrelent: Jour. de méd. de Bordeaux **26**:502 and 542, 1896.

31. Gory, M., and Dalsace, J.: Infection typhoïde du cobaye par inoculation sous-coutanée de culture. Infection transplacentaire du foetus, Compt. rend. Soc. de biol. **95**:1530 (31 Déc.) 1926.

32. DeLee, J. B.: Infection as Causes of Stillbirth and Sundry Obstetric Theories, Bull. Lying-in Hosp. N. Y. **11**:1 (Jan.) 1917.

fever and were removed to the isolation hospital. The mother was warned to keep away from the children. Ten days later, a baby was born; desquamation was occurring over the whole trunk and limbs. This continued for several days, and the urine showed distinct traces of albumin. The child recovered. The mother did not have a sore throat or rash and her temperature was normal, but at the age of 10 years she had had a severe attack of scarlet fever.

Evidently, no organ is immune to prenatal influences. We find that Graham [33] recognized pyelitis in the newly born, recording one case in which the intra-uterine development of the disease was unquestionable.

SUMMARY

Maternal infections bear an important influence on fetal viability and mortality. The transmission of a general infection takes place through the maternal blood vessels to the circulation of the fetus through apparently unruptured vascular channels. Practically all known specific diseases have been encountered.

Two cases of pneumococcic infections are reported. One occurred during a pneumococcic puerperal septicemia and produced a similar bacteremia in the fetus. In the second case, the mother is living and well, but the dead-born fetus showed an old syphilitic fibrous peritonitis on which a recent pneumococcic infection was superimposed. During pregnancy, the mother had a sore throat one week before delivery. During the puerperium when cultures were taken, pneumococci were isolated among other organisms. This case and others recorded bring out in a pronounced manner the fact that maternal bacterial carriers at times produce relatively little if any ill effects; yet by lowering the general resistance, the status of the fetus at times is influenced extremely unfavorably.

A review of the literature and our own cases bring to the forefront the importance of the maternal prenatal care. Even such momentarily insignificant minor disabilities as sore throats and colds should receive the most careful attention.

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33. Graham, R. H.: A Report of Six Cases of Pyelitis in the Newly-Born Infant, Am. J. M. Sc. **170**:401 (Sept.) 1925.

THE PHARYNGEAL TONSIL*

W. E. COOKE, M.D.
Director of the Pathologic Department, Wigan Infirmary
LANCASHIRE, ENGLAND

This communication summarizes the observations of a research on the embryology, bacteriology and pathology of the pharyngeal tonsil.

EMBRYOLOGY

Behind the oral plate in the middle line of the roof of the pharynx, anterior to the basioccipital, there is a depression called Sessel's pocket. Its embryologic significance is not understood, but it may be the remains of the pharyngeal opening of the notochord. In and around this recess, the pharyngeal or Luschka's tonsil develops.

About the fourth month of fetal life, faint striae appear on this part of the posterior pharyngeal wall, and microscopic examination shows the tissue to consist of reticular tissue enclosing in its meshwork a few scattered lymphocytes. Development of this diffuse lymphoid tissue continues in the superficial fibers of the tunica propria of the pharyngeal mucosa until at 5½ months the pharyngeal tonsil appears as a definite organ. Mucous glands are developed at the base and early formation of lymph vessels is seen (fig. 1). The epithelium covering the organ is still of the rudimentary type, rounded or ovoid cells, two or three layers in thickness resting on a delicate basement membrane.

At 6½ months (fig. 2) the lymphoid tissue has increased, the epithelium is from 2 to 4 cells deep, the basement membrane well defined, and the superficial cells have become differentiated into the columnar ciliated type. Early formation of crypts is seen. The mucous glands have increased in number, and the tonsil is a fully functioning organ at the time the child is viable.

At term (fig. 3), the pharyngeal tonsil appears as from four to six molds of lymphoid tissue suspended by its capsule to the roof of the pharynx. The leaflets are not separate as in the hypertrophoid adenoid, but appear as longitudinal rugae set on a deep base of lymphoid tissue. The crypts have undergone further development and mucus bathes their surface and is contained within them.

Lymphocytes have already commenced to migrate between the epithelial cells and lie free in the mucus. Germ centers are not definite, but are represented at this stage as small, loose aggregations of lymphoblasts.

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* Received for publication, Oct. 4, 1927.

* The word "tonsil" is used here to denote the pharyngeal tonsil only.

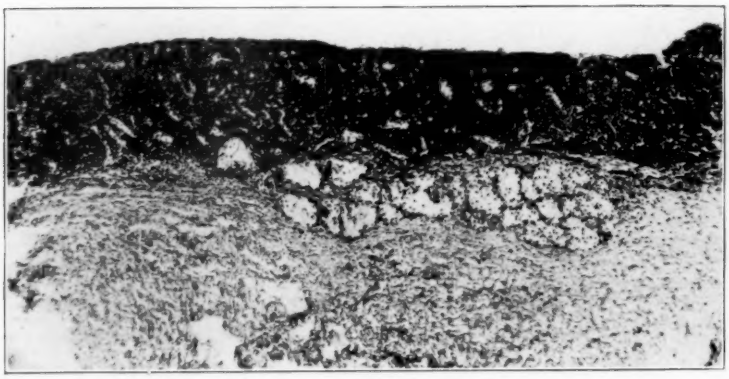

Fig. 1.—Pharyngeal tonsil of fetus of 5½ months, showing early formation of mucous glands. The covering epithelium has not yet become differentiated into the ciliated type; × 65. The photomicrographs were made by W. E. Cooke and C. F. Hill.

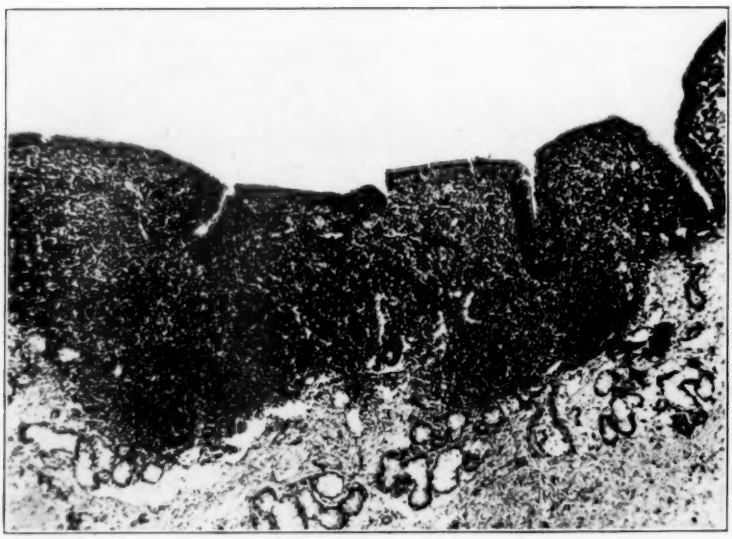

Fig. 2.—Pharyngeal tonsil of fetus of 6½ months. The lymphoid tissue has increased in thickness, early crypt formation is seen, and the epithelium is columnar ciliated; × 65.

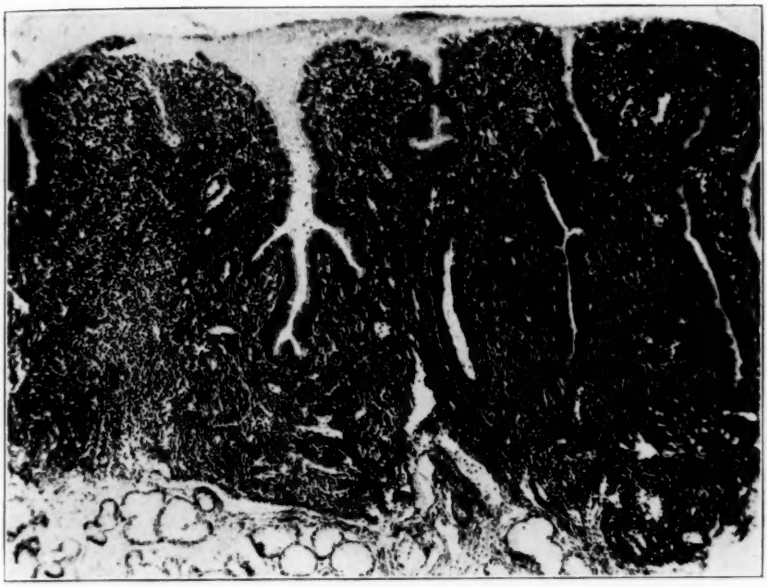

Fig. 3.—Pharyngeal tonsil at term. Crypt formation is well shown, the tonsil is bathed in mucus in which lymphocytes are seen; × 65.

Fig. 4.—Hypertrophied tonsil showing prominent germ centers and a large cyst; × 10.

The epithelial cell layer has become more sharply defined, and the basement membrane is seen to consist of flattened cells of the corium—a stratum of condensed reticular tissue. In the lymphoid mass are seen blood capillaries and lymphatic vessels.

In the capsule or base are blood vessels, mucous glands, ducts and lymphatics.

During the first few months of infancy, well defined germ centers appear as in other parts of the pharyngeal lymph ring and in the lymphatic tissue elsewhere. The organ increases in depth, owing to further development of the crypts, and the superficial area is increased.

In neither the fetus nor the normal tonsil of infancy were any bodies corresponding to Hassal's corpuscles of the thymus found. This point will be mentioned again under "pathology."

PHYSIOLOGY

Many functions have been ascribed to the pharyngeal tonsil—protective, internal secretory, hemopoietic, elimination and the production of immunity—but there is no reason to believe that the lymphoid tissue of the adenoid differs from that in other parts of the organism.

Its histology and position, however, suggest a special function. Histologically, it is a lymphoid mucus secreting organ presenting the arrangement of crypts for increasing its superficial area, and, unlike any other component of Waldeyer's ring, its surface is covered with ciliated epithelium. Anatomically, it is situated in the direct path of inspired air, in the area innervated by the glossopharyngeal nerve and Meckel's ganglion. These facts at once suggest the function of a surface filter for inspired air, and a first line of defence. We believe these to be its only special object.

The glossopharyngeal vagal connection is not sufficiently understood, but probably plays an important part in the production of the syndrome of the child with hypertrophied adenoids.

As Sturm [1] points out the effects of hypertrophy of Luschka's tonsil are not due to mechanical obstruction to respiration, as there is no obstruction between the outer air and the glottis, and the child can still breathe through the mouth.

In addition to the toxemia from which these children undoubtedly suffer, there must be some other factor present in the child with hypertrophied adenoids to account for the area of pulmonary collapse, thoracic deformity and defective apical ventilation so commonly found. Sturm suggests reflex intervention with the normal respiratory rhythm; if the problem is considered from all points, few will disagree with him.

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1. Sturm, F. P.: The Pharyngeal Lymph-Ring, Medical World, 1927, vol. 1.

BACTERIOLOGY

Our results merely confirm those obtained by others who have investigated the flora of the nasopharynx. The common organisms found in the hypertrophied tonsil removed at operation were: *Streptococcus hemolyticus, Streptococcus viridans, Micrococcus catarrhalis,* pneumococcus, *Staphylococcus aureus* and *albus, Micrococcus flavus* and diphtheroids.

Inoculation experiments to discover the presence of the tubercle bacillus were not undertaken, but the fact may be recorded that in the hundreds of specimens examined microscopic evidence of this bacillus was not found, nor was there any histologic evidence of tuberculous

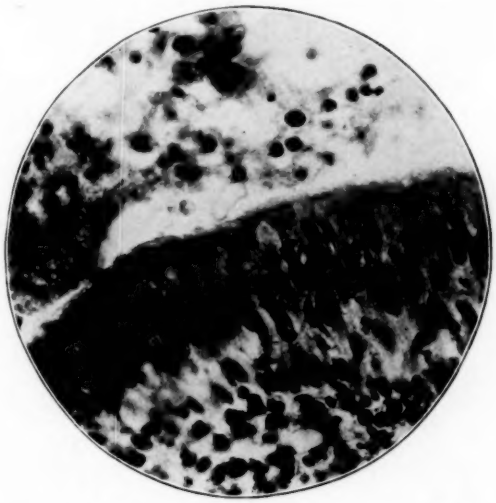

Fig. 5.—Ciliated epithelium covering the surface of the pharyngeal tonsil; × 400.

infection in the several thousands of sections examined. That the tubercle bacillus does occur in the adenoid is proved by the one or two published cases, but the infection is extremely rare.

PATHOLOGY

The condition which attracts attention and invites surgical intervention is hyperthrophy. In acute leukemia and lymphatism, for example, and under conditions less definite and even less understood, hyperthrophy of the pharyngeal tonsil takes place as a part of a general lymphatic hyperplasia. As the tonsil is continually receiving massive doses of organisms on its surface, it is reasonable to suppose that some gain entry through the covering of the germicidal mucus.

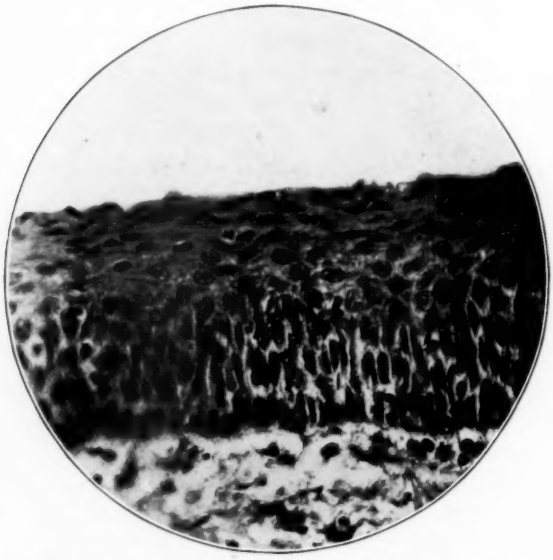

Fig. 6.—Stratified epithelium of the hypertrophied organ; × 400.

Fig. 7.—Cyst formation. The epithelium is seen to be ciliated in the early cyst, and the contents consist of mucus, desquamated epithelium, and lymphocytes; × 50.

Given the unknown factor, these repeated infections would cause reaction in the lymphoid mass which would result in hyperthrophy. The enlargement is due entirely to hyperplasia of the lymphatic elements (fig. 4). The germ centers are large and prominent, and the reticular stroma is densely packed with lymphocytes. As a result of this hyperplasia, several conditions occur. The normal columnar ciliated epithelium on the external surface (fig. 5) becomes stratified (fig. 6), but the cryptal epithelium for the most part retains its ciliae.

Cyst formation takes place owing to occlusion of the whole or part of a crypt (figs. 4. 7 and 8). The epithelium lining an early cyst is still ciliated (fig. 7) but soon undergoes mucoid degeneration (fig. 9);

Fig. 8.—Cyst at a later stage, showing the homogeneous laminated contents; × 50.

finally, the nuclei of the desquamated cells and lymphocytes disappear, leaving the contents homogeneous (fig. 8). The surrounding epithelium is represented by layers of flattened nuclei (fig. 10) resting directly on lymphoid tissue without any attempt at the formation of a fibrous capsule. Concentric corpuscle formation is seen. These are laminated bodies, "nests" of flattened epithelium (fig. 11). The mode of formation appears to be as follows:

Small islets of epithelium at the angles of crypts become isolated by pressure of the hypertrophied lymphatic mass, the innermost cells degenerate, and the outer whorls of the nest are composed of compressed flattened epithelial nuclei.

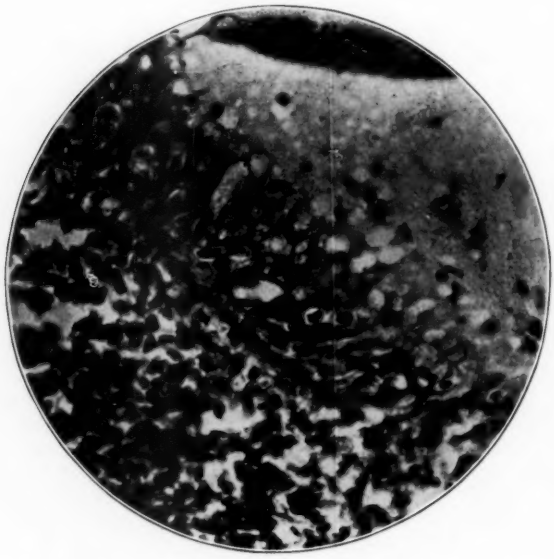

Fig. 9.—Wall of cyst (fig. 7) showing mucoid degeneration of the lining epithelium; × 400.

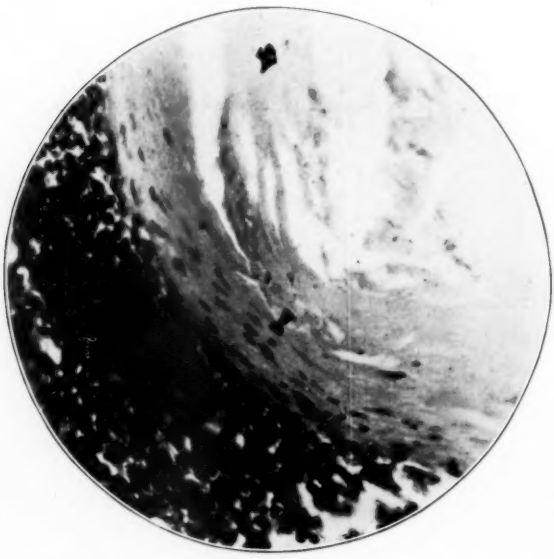

Fig. 10.—Wall of cyst (fig. 8) showing flattened epithelium; × 400.

Fig. 11.—"Cell nest;" × 400.

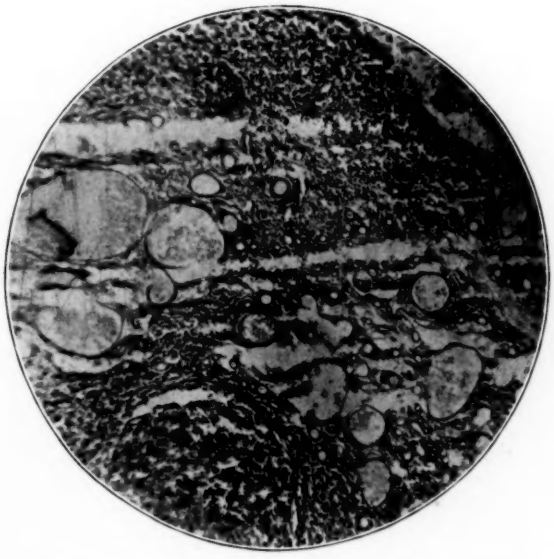

Fig. 12.—Fibrosis at the capsule showing dilated vessels; × 50.

In this category of pressure effects should be included fibrosis of the basement membrane of the epithelium, which is a constant feature of the adenoid, and is probably due to interference with its supply of blood. Marked fibrotic changes are rare, except in the capsule. In addition to fibrosis of the epithelial basement membrane, there is hyperplasia of the reticular tissue of the germ centers and of the cores of the leaflets, but replacement fibrosis in the accepted sense of the term takes place only after abscess formation.

The base, or capsule, however, frequently shows a marked increase in fibrous tissue in which periarteritis, endarteritis and dilation of the veins are prominent (fig. 12).

As adolescence approaches, the organ diminishes in size by numerical diminution of the germ centers and lymphocytes with corresponding prominence of the reticular tissue.

Abscess formation is seen as a collection of polymorphus, plasma cells and monocytes intermingled with lymphocytes of the tissue. The epithelium overlying the abscess undergoes necrosis, and an ulcer exuding pus containing these cells results. The base of the ulcer at first is composed of the lymphatic tissue of the organ, fibrosis of the area taking place later.

The foregoing are the salient facts concerning the development and pathology of the pharyngeal tonsil, but any contribution about the problem of the child with hypertrophied adenoids would not be complete if it did not contain an appeal for proper treatment as soon as the diagnosis of hypertrophy is made. Hypertrophy of Luschka's tonsil is an important pathologic state, fraught with such immediate and remote dangers that it is a national duty to place the sufferer under skilled supervision at the earliest moment.

Case Reports

ACUTE MASSIVE ATELECTASIS OF THE LUNG

COMPLICATING A FRESH TUBERCULOUS PRIMARY COMPLEX *

E. GORDON STOLOFF, M.D.
NEW YORK

In recent years massive collapse (atelectasis) of the lungs has ceased to be regarded as a rare occurrence, and this is largely due to the universal use of roentgenography, which has become so indispensable an adjunct in clinical diagnosis. The type of collapse of the lung now under consideration is that which occurs in a lung that was previously normally aërated, with normal anatomic landmarks, in which a sudden cessation of the intake of air, with a consequent atelectasis of the alveolar tissue results from some disturbance in the bronchial tree as obstruction, occlusion or obturation. This is differentiated from the type of collapse or atelectasis which is secondary to pneumothorax, effusion or tumorous masses compressing and displacing alveolar tissue and bronchi as well. The collapse may be partial or total, depending on the amount of alveolar tissue involved, so that there may be a collapse of the entire lung, a lobe, a part of a lobe, parts of different lobes or parts of two different lobes, one on each side. This variation will, of course, depend on whether the main bronchus is involved or only subdivisions thereof on the same side or both sides.

The subject of massive collapse of the lung has been described and discussed by Pasteur,[1] Rose-Bradford,[2] Briscoe,[3] Lichtheim,[4] Elliott and Dingley,[5] Grailey and Hewitt,[6] Meyer,[7] Abt,[8] Norris and Landis,[9]

* Received for publication, Aug. 13, 1927.

* From the Pediatric Service (Dr. B. Schick) and the Radiological Service (Dr. L. Jaches), Mount Sinai Hospital.

* Presented at the Pediatric Section of the New York Academy of Medicine, March 17, 1927.

1. Pasteur: Middlesex Hosp. Rep., 1910; Collapse of the Lung, Brit. J. Surg. **1**:587, 1914.

2. Rose-Bradford: Massive Collapse of the Lung, Oxford Loose Leaf System of Medicine, vol. 2, p. 127.

3. Briscoe: Collapse of the Lung, Quart. J. Med. **13**:293, 1920.

4. Lichtheim: Arch. f. exper. Path. u. Pharmakol. **10**:54, 1878.

5. Elliott and Dingley: Massive Collapse of the Lung, Lancet **1**:1305, 1914.

6. Grailey and Hewitt: Massive Collapse of the Lung, Reynold System of Medicine, 1871, p. 865.

(Footnotes continued on following page)

McCrae,[10] Holmes [11] and others. Recently the subject has been thoroughly studied by Chevalier Jackson,[12] Jackson and Lee,[13] Manges [14] and Sante.[15] On the basis of these and my own studies, the etiology may be considered as being of three types: (1) intrabronchial, (2) extrabronchial and (3) idiopathic.

In the bronchial type is found an obstruction within the bronchus which may be caused by a foreign body or tissue or by an exudate acting as a foreign body. These may be: organic (beans, seeds, nuts or their kernels, etc.), inorganic (metallic objects, marbles, etc.), plugs of mucus or of pus (Churchill and Holmes [16]) or tumors (polypi, squamous-cell carcinoma [16]).

The clear comprehension of this group has been created by the expert work of Chevalier Jackson and his co-workers, who have shown repeatedly that collapse of the lung to varying degrees may be caused by foreign bodies.

Jackson [17] classifies intrabronchial obstruction in three types: (1) by-pass valve type, in which the ingress and egress of air is permitted, thus causing neither collapse nor emphysema in the tributary lung, (2) check valve type, in which ingress of air is permitted, but egress prevented so that an obstructive emphysema of the tributary lung results and (3) stop valve type, in which ingress and egress of air is not permitted, while the absorption of the already present alveolar air results in total atelectasis of the lung.

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7. Meyer, Willy: Massive Collapse of the Lung, M. J. & Record **82**:1256, 1924.

8. Abt, I. A.: Massive Collapse of the Lung, Am. J. Dis. Child. **30**:347 (Sept.) 1925.

9. Norris and Landis: Diseases of the Chest, Philadelphia, W. B. Saunders Company, 1922, p. 487.

10. McCrae, T.: Physical Signs of Foreign Bodies in Bronchi, Am. J. M. Sc. **159**:313 (March) 1920; Lumelian Lectures, Lancet **1**:735, 787 and 838 (April 2, 19 and 26) 1924.

11. Holmes, G. W.: Massive Collapse of the Lung, Am. J. Roentgenol. **11**: 509, 1924.

12. Jackson, C.: Foreign Bodies in Bronchi, referred to in Billings, F., and Forchheimer: Therapeusis of Internal Diseases, New York, D. Appleton & Company, 1924, vol. 5, chapter 4, p. 72.

13. Jackson and Lee: Acute Massive Collapse of the Lung, Tr. Am. Lung A. **43**:723, 1925.

14. Manges, W.: Roentgen-Ray Diagnosis of Non-Opaque Foreign Bodies, Am. J. Roentgenol. **9**:288, 1922.

15. Sante, L. R.: Massive Collapse of the Lung, Radiology **8**:1 (Jan.) 1927; J. A. M. A. **88**:1539 (May 14) 1927.

16. Churchill, E. D., and Holmes, G. W.: Lobar Atelectasis in Chronic Pulmonary Suppuration, Arch. Surg. **14**:1093 (May) 1927.

17. Jackson, C.: Pulmonary Collapse Due to Foreign Bodies in the Bronchi, Tr. Am. Lung A. **43**:39, 1925.

In the extrabronchial type of obstruction, the lung may suffer from a sudden airlessness, following compression of the bronchus by lymph glands or tumors situated outside the bronchus. Such compression may cause bronchial obstruction in the same way as the intrabronchial group, that is the by-pass valve type, the check valve type or the stop valve type.

The idiopathic group of cases of total atelectasis includes a number of cases reported, in which there has not been a history, apparently, of aspiration, of the presence of foreign body or of bronchial compression. Most of these have followed operative procedure in various parts of the body, under local as well as general anesthesia. The following hypotheses have been offered to explain such instances of collapse of the lung: 1. It is caused by some disturbance or injury to the phrenic nerves, according to Briscoe,[3] Martin and Hare [18] and Schroeder and Green.[19] 2. Elliott and Dingley [5] suggest that immobilization of the thoracic wall and diaphragm permits the collection of secretion in the bronchial tree to such an extent that the admission of air is prevented, while the already contained alveolar air is absorbed, leading to collapse. Rose-Bradford [2] and Meyer [7] feel that posture and insufficient expansion play, perhaps, the most vital rôle. Jackson,[17] Lichtheim [4] and Manges [14] feel that obstruction within the bronchial tree is the etiologic factor. Jackson,[17] however, believes that immobilization of the chest and posture are probably added or contributory factors.

Sante [15] believes that injury to the vagus nerve causes a reflex spasm of the bronchioles, with a resulting airlessness of the lungs. In support of this theory he presents cases in which a history of operative procedure or of the presence of a foreign body has not been obtained. It is noteworthy, however, that in many cases in which collapse of the lungs was present, especially following operations, a restitution of the lungs, at times to normal aëration, was produced by Jackson by removal of mucous plugs in the bronchial tree. I feel that the number of such cases, which are called idiopathic collapse of the lungs will progressively become smaller as the number of thorough, reliable bronchoscopies increases.

REPORT OF CASE

The case presented in this article is of interest chiefly because of the age of the child, and because of the total collapse of the left lung which complicated a fresh tuberculous primary complex in the lungs.

History.—F. D., a girl, aged 2 years, of Italian parentage, had a past history which was essentially negative. Development had been normal. Five days before admission to the hospital, the child was restless and irritable, and the temperature was said to have been elevated. For the four days following, up to admission, the fever persisted, and she remained restless and irritable. She

18. Martin and Hare, quoted by Jackson and Lee (footnote 13).

19. Schroeder and Green: Am. J. M. Sc. **123**:196, 1902.

refused all food and coughed slightly. There was some respiratory embarrassment. A history of the aspiration of a foreign body could not be elicited. The child was well nourished. She was irritable and restless, and had slight dyspnea. Signs in the chest were dulness anteriorly as low as the fourth rib and posteriorly to the angle of the scapula. Over the same region, the breath sounds were faintly tubular. Râles were not heard. The apex of the heart was percussed 2 cm. to the left of the middle line. The temperature was 104 F. A provisional diagnosis of pneumonia of the left upper lobe, with dilatation of the heart, was made. On the following day the temperature decreased to 100 F.

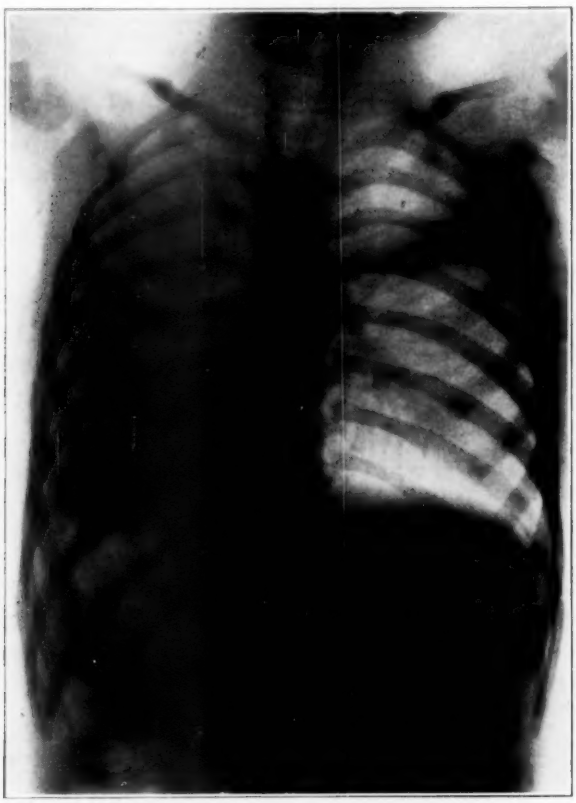

Fig. 1 (Feb. 21, 1927).—Roentgenogram showing massive atelectasis (collapse) of the left lung with compensatory emphysema of the right lung.

The child was comfortable. The chest showed dulness anteriorly and posteriorly over the same region as on the previous day, and added to that, flatness over the base, where, however, the voice sounds were bronchial. Râles were not heard. Coughing was only occasional from the time of admission, and mucus or sputum had not been produced. A diagnosis was made of pneumonia of the left upper lobe with pleural effusion over the base. A roentgenogram was ordered. On the following day, fever was not present, and the signs disappeared almost completely, except for some dulness in the left interscapular region. The Pirquet reaction was now interpreted as positive.

Roentgen-Ray Diagnosis.—The roentgenogram taken on the previous day was now reported as follows," There is an homogenous, fairly dense shadow, occupying the entire left thoracic cavity. The diaphragm of the same side is slightly elevated. The heart is displaced into the corresponding (left) side so that its margins are not visible. The trachea is displaced toward the same side. The right thoracic cavity appears larger than the left. Part of the emphysematous right lung can be seen protruding into the left thoracic cavity. The right diaphragm is flattened and lowered. There is no evidence of opaque foreign bodies. The roentgen appearance is that of total or massive atelectasis of the lung, the etiology of which cannot at present be determined." On the

Fig. 2 (Feb. 25, 1927).—Roentgenogram showing the restitution of the collapsed left lung to normal aëration. The primary infect is visible with disease of the regional lymph gland.

third day after admission, the temperature was normal, and it remained so until the seventh day, when a sudden rise occurred. On this day, too, a roentgenogram showed a complete restitution of the heart and superior mediastinum to normal position. "The trachea is now in the midline. The left lung shows normal aëration, except for one small, circumscribed, fairly dense shadow, about the size of a dime, lying midway between the cardiac margin and the lateral thoracic wall, at about the level of the fourth interspace anteriorly, which may be due to incomplete aëration of the lung resulting from the recent complete atelectasis. The presence of the positive Pirquet reaction in

a child of this age suggests, however, the possibility that this area which looks like infiltration may be due to primary tuberculous infection of the lung."

The only physical sign in the lungs on this day was some dulness in the left interscapular region, immediately above the angle of the scapula. The breath sounds were faintly bronchial. The sudden rise in temperature could not be explained until it was discovered that by some error an intracutaneous tuberculin test was performed on this child who reacted positively to the Pirquet reaction, or, in other words, 1 mg. of old tuberculin was injected into this child who had already demonstrated the presence of tuberculous infection by reacting to 0.00001 Gm. of old tuberculin (Pirquet test). The fever persisted for three days, the temperature remaining normal thereafter, except for one or two rises due to nasopharyngitis.

Frequent roentgenograms have been taken since, at intervals of about a week. The essential points are illustrated in figure 3.

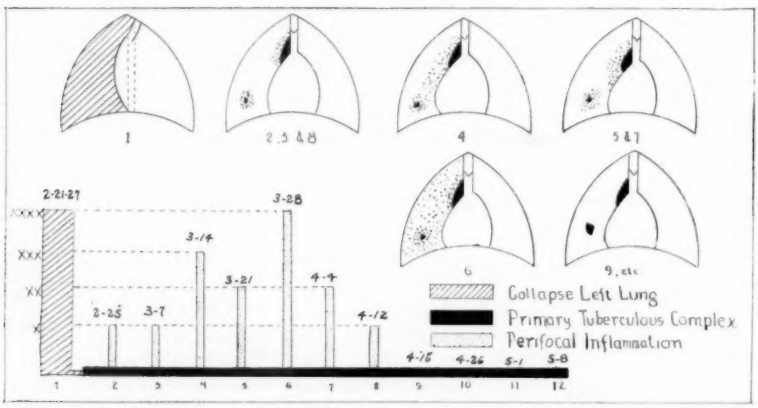

Fig. 3.—Diagrammatic representation of the roentgenograms illustrating the primary tuberculous complex and perifocal inflammation.

There are four characteristic signs of total atelectasis of a lung. They are the signs of bronchial stenosis, regardless of the etiologic factor: (1) complete airlessness of the lung, (2) elevation of the diaphragm of the same side, (3) displacement of the heart and superior mediastinum toward the affected side, as noted particularly in the displacement of the trachea, and (4) compensatory emphysema of the opposite side. These signs are all present in the first roentgenograms, making the diagnosis unequivocal.

In a recent publication [20] I have taken up in detail the roentgen-ray diagnosis of the primary tuberculous complex in the lung during childhood. Roentgenograms of a patient were cited in which a primary tuberculous complex was followed from its inception, over three years and four months, until definite healing, as evidenced by calcification, was

20. Stoloff, E. Gordon: Primary Infection in Tuberculosis, Am. J. Dis. Child. **33**:363 (March) 1927.

present. It was pointed out that both roentgenograms and fluoroscopes were to be used and that certain signs must be present for a definite roentgenologic diagnosis: (1) positive tuberculin skin reactions; (2) primary focus of infection clearly visualized; (3) diseases of the regional lymph gland, and (4) evidences of lymphatic connection between the primary focus and the regional lymph glands, and of pleuritic involvement, which are helpful, but not essential for diagnosis.

I stated that it is well to consider the primary infection in three stages: (1) the beginning stage, (2) the progressive stage and (3) the healing stage, or healed stage.

Since in this case the picture is that of the beginning stage, which may probably be passing into the healing stage, I shall consider only the beginning stage. Shadows caused by the primary infect may not be seen in this early stage, since the area may be so small, and the stage of exudation and productivity may be so limited as to be insufficient to cause any shadows. On the other hand, the area may be the size of a walnut or may even occupy the entire lobe. Such an extensive involvement, it must be understood, is not caused by the primary infection per se, but rather by an associate collateral inflammation. The roentgenogram of a primary tuberculous infection may not show any essential difference from that of a bronchopneumonic infiltration. A positive reaction to tuberculin, however, evident disease of the regional lymph glands of the hilum, the age of the patient, the history of exposure and the clinical course and appearance help to establish the diagnosis of primary infection of the lung.

The course in the lymph glands of the hilum is similar to that in the infection, but it is usually much more intense and extensive. There may be inflammation around the focus in the lymph gland itself, and it may extend to the connective tissue, the bronchi, the interlobular fissures and septums in the adjacent tissue of the lung. This perifocal inflammation consists of a serous lymphocytic exudation which has been called collateral inflammation (Tendeloo),[21] perifocal inflammation (Ranke),[22] gelatinous infiltration (Fraenkel),[23] epituberculosis (Eliasberg and Neuland) [24] and paratuberculosis (Engel).[25] These various names all designate a more or less chronic inflammation surrounding a tuberculous

21. Tendeloo: Allgemeine Pathologie, Berlin, J. Springer, 1919.

22. Ranke: Zur Diagnose der kindlichen Tuberculose, München. med. Wchnschr. **27**:2099, 1914.

23. Fraenkel: Pathologische Anatomie, Kaufmann's **1**:341, 1922. Berlin V. W. V.

24. Eliasberg, H., and Neuland, W.: Die epituberkulöse Infiltration der Lunge bei tuberkulösen Saüglingen und Kindern, Jahrb. f. Kinderh. **93**:88, 1920.

25. Engel: Ueber paratuberkulöse Lungenerkrankungen, Klin. Wchnschr. **42**:877 (Jan.) 1921.

focus in the tissue of the lung or lymph glands of the hilum, which is probably caused by a tuberculotoxic reaction. This perifocal inflammation is usually present around the fresh primary focus and also adjacent to the fresh tuberculous infection of the lymph glands of the hilum (a primary tuberculous infiltration) (Simon and Redeker).[26] It also not infrequently occurs with such infections of older age (a secondary tuberculous infection) (Simon and Redeker).[26] This perifocal inflammation, or epituberculosis, as it is frequently called, is specific in the sense that it is secondary to, and associated with, tuberculous infection. It is, however, nonspecific in the sense that it does not contain tubercle bacilli. It is a tuberculotoxic reaction. This reaction may be considered benign or malignant. It is usually benign, since healing occurs with little, if any, residue. If, however, tubercle bacilli gain entrance into this inflammatory area, specific tuberculous disease may result with its usual course, i. e., caseation, cavitation and calcification.

The shadow then present at the hilum is caused by two factors: (1) enlargement and swelling of the lymph glands of the hilum, due to tuberculous diseased tissue with perifocal inflammation added thereto and (2) perifocal inflammation in the tissue of the lung adjacent to the lymph glands.

The appearance of the roentgenogram may vary:

1. Dense shadows, varying in size, may be present in the region of the hilum. They may be sharply circumscribed, oval or circular and notched or uninterrupedly circular, owing to the glands. Continuous with them is a shadow of lesser density which gradually fades into the lung of normal density, and which is caused by the collateral perifocal inflammation.

2. There may be present in the region of the hilum, only a wing or fan-shaped shadow, of varying density, which fades gradually into the lung and in which definite evidence of glandular structure is not noted. This may be a shadow of the lymph glands themselves, with or without perifocal inflammation. It must be remembered that diseases, other than tuberculosis (pneumonia, Hodgkin's disease, leukemias, tumors and others) may cause exactly such a shadow; therefore, all other clinical facts must be considered. Interlobar thickening and exudation are associated with a primary tuberculous focus, and with its regional lymph glands of the hilum not infrequently. They may produce a shadow at the hilum, which is usually triangular. I [20] have previously emphasized the importance of complete fluoroscopy and of roentgenograms taken with the patient in various positions in order to diagnose or to exclude such an involvement.

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26. Simon and Redeker: Praktisches Lehrbuch der Kindertuberkulose, Leipzig, Curt Kabitzsch, 1927, p. 157.

COMMENT

In the case herein reported several facts became evident from the study of the roentgenograms: 1. Two shadows were constant throughout the course: (*a*) One was in the field of the left lung in the lower part of the left upper lobe. It was about the size of a dime, was of increased density and was more or less sharply circumscribed. This was, probably, the primary tuberculous focus. (*b*) In the region of the hilum was seen a fairly dense, fan-shaped shadow, opposite and slightly above the level of the shadow in the lung field just described. This probably indicated the disease of the regional lymph gland. 2. Shadows of varying extent appeared and disappeared around both parts described in (*a*) and (*b*), and these were caused by perifocal inflammation.

In view of the age of the patient and the strongly positive Pirquet reaction, a diagnosis of a fresh tuberculous primary complex of the lung was justifiable. I believe that the complex was fresh because of the age of the child, the appearance of the primary infection and the hilum in the roentgenogram and the absence of what might be interpreted as caseation and cavitation or calcification. The last roentgenogram presented the appearance of a primary tuberculous complex in the stage of bipolarity, as designated by Simon and Redeker,[26] the two poles being the primary tuberculous infect and the regional lymph gland, respectively.

This case then, was one of a young child, aged 2 years, who was suffering from a primary tuberculous infection of the lung. The regional lymph glands were involved to such an extent as to contribute to the causation of a stenosis of the bronchus, with resultant massive atelectasis of the left lung. The stenosis was likely caused, mainly, by direct compression by pathologic lymph glands and was aided, probably, by an associate perifocal inflammation of the bronchial wall, which caused narrowing. Added to that, exudate or mucus might have been present within this narrowing. A subsidence in the extent of the inflammation caused a return of the patency of the bronchus, with a restitution and reaëration of the lung. Instances of atelectasis of parts of the lung, following pressure of tuberculous lymph glands, have been observed by Schick,[27] Simon and Redeker,[26] Duken [28] and Lerche.[29] Only after restitution of the collapsed area and the subsequent study of the roentgenograms could the etiologic cause of the atelectasis in the case cited be ascertained.

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27. Schick: Personal communication to the author.

28. Duken: Die Besonderheiten der roentgenologischer Thorax-Diagnostik im Kindesalter, Jena, Gustav Fischer, 1926, p. 67.

29. Lerche: Infected Mediastinal Lymph Nodes as a Source of Mediastinitis, Arch. Surg. **14**:285 (Jan.) 1927.

The physical signs were never definite or helpful. The dulness and bronchial breathing found on admission anteriorly and posteriorly in the upper part of the left lung, and the dulness and diminished and faintly bronchial breathing heard in the lower part of the left lung on the day following, were the only definite signs, and these were found during a stage of total atelectasis of the lung. It is characteristic of total atelectasis that the signs are not commensurate with the amount of lung tissue collapsed. The degree of bronchial breathing will vary directly with the patency of the bronchi and the amount of air contained therein. After the restitution of the lung to its normal landmarks, only a suggestion of dulness in the left interscapular region was elicited. In this case, as in many others, I have not been able to utilize with advantage the percussion of the spine (Koranyi), the spinalgia (Petruschky), the spinotracheal breathing (Wallgreen) or the D'Espine sign, all of which have been described as being characteristic in tuberculous swelling of the tracheobronchial glands. A diagnosis of dilatation of the heart is not infrequently made when the massive atelectatic process is not on the left side, for the heart is displaced so that the apex is far beyond its normal limits. In my case, the same error was made.

Bronchoscopy is an invaluable aid in all cases of collapse of the lungs, by which foreign bodies, if present, may be removed, or the bronchus may be cleared of any secretion or mucous plugs; it also helps to establish a diagnosis. In the case cited, a bronchoscopy was not performed because of the age of the child, because the general condition was so much improved and because the lung was rapidly restored to normal. In view of these facts, it did not seem justifiable to submit such a young child to a bronchoscopy.

SUMMARY

1. Acute massive atelectasis of the lungs is considered as being caused by some disorder centering, primarily, about the bronchus. It may be: (*a*) an intrabronchial obstruction, (*b*) an extrabronchial obstruction or (*c*) an idiopathic obstruction.

2. Intrabronchial obstruction and also extrabronchial obstruction may be of the by-pass valve type, the check valve type or the stop valve type.

3. A case is presented of a girl, aged 2 years, who suffered acute massive atelectasis of the lung resulting from extrabronchial, as well as intrabronchial, causes.

4. The basic cause of the atelectasis was the enlargement of the regional lymph nodes caused by a fresh primary tuberculous complex, this enlargement being marked enough to occlude the already inflamed bronchus, with subsequent atelectasis of the lung. Plugs of exudate or mucus may also have been present.

5. Perifocal or epituberculous inflammation surrounding the tuberculous primary focus or the regional lymph gland of the hilum was discussed.

6. Study of all the clinical details emphasizes the fact that the most important and valuable single adjunct in the diagnosis either of acute massive atelectasis of the lungs or of the primary tuberculous complex is roentgen-ray examination, including fluoroscopy.

1085 Park Avenue.

PULMONARY GANGRENE FOLLOWING DIPHTHERIA

REPORT OF A CASE *

CHARLES T. OLCOTT, M.D.
AND
JOHN G. MERSELIS, M.D.
NEW YORK

We report the following case of pulmonary gangrene subsequent to diphtheria because a review of the literature has not revealed a case with this etiology.

REPORT OF A CASE

Clinical History.—M. C., a colored girl, aged 15, was admitted to the wards of Willard Parker Hospital, Feb. 27, 1927, on the third day of her illness. Her family history was negative. At practically the same time, two other children were admitted to the hospital with diphtheria; both recovered without complications. The patient's past history was negative except for measles, pertussis, varicella and mumps in early childhood.

Two days before admission, the patient complained of having a sore throat, and it was thought that she had some fever. The next day she vomited and complained of increasing pain in her throat.

Examination.—On February 27 at 4 p. m., she was brought to the hospital in an ambulance acutely ill. Physical examination revealed: eyes and ears normal; nose, completely obstructed posteriorly; no nasal discharge; tongue, dry and coated; no Koplik's spots; marked edema of the soft palate, posterior pharyngeal wall and peritonsillar regions. The tonsils were greatly hypertrophied. There was an extensive gray membrane covering the soft palate, uvula, anterior and posterior pillars, posterior pharyngeal wall and both tonsils. The submaxillary glands were palpable; the anterior and posterior cervical lymph nodes were greatly enlarged and slightly tender, firm and confluent, giving the patient the typical "bull-neck" appearance so commonly seen in cases of toxic diphtheria. She held her mouth open, spoke with difficulty and expectorated a clear saliva at frequent intervals, because of the pharyngeal edema and associated dysphagia. Changes of the voice or true dyspnea suggestive of laryngeal or tracheal involvement was not present. The lungs were clear to percussion and auscultation; the heart borders were within normal limits, the sounds were distant but clear, the rhythm regular, the rate 128. Her pulse was rapid and soft. Examination revealed that the abdomen and extremities were normal, as were the reflexes and other neurologic phenomena. The skin was normal in texture, and there were no eruptions. The respiration was 28; the temperature, by rectum, 103.6 (39.7 C.). The diagnosis on admission was tonsillar, faucial, toxic diphtheria.

Treatment and Course.—Having been tested and found not to be sensitive, the patient was given diphtheria antitoxin, 15,000 units intravenously and 10,000 units intramuscularly. Warm throat irrigations of 1 per cent boric acid in saline solution were given at frequent intervals on the first day, but were discontinued on

* From the laboratory of the Willard Parker Hospital.

the second, as the patient was comatose. Her condition remained unchanged for three days. She labored for breath, was stuporous, disoriented and aroused only to take fluids and nourishment. The temperature had fallen to 100.6 F. (38.1 C.) on the day after admission, but rose the next day to 105 (40.5); it remained thus for four days, in spite of attempts to reduce it.

On the fifth day after admission, the patient appeared brighter, took fluids and nourishment well, and did not complain. The membrane over the soft palate and uvula had begun to loosen about the periphery. The lungs remained clear and the heart sounds distant, but regular.

On the following morning, improvement was even greater, with a decrease in the pharyngeal edema and swelling of the cervical lymph nodes. At 6:30 p. m., she complained of having a sharp pain in her right side. The respiratory rate increased to 40. Examination at this time did not reveal a change in percussion note, but a faint pleural friction rub was heard in the right axillary line at the base of the lung. Adhesive strapping was followed by relief of pain.

The next day, although the patient was subjectively relieved, a frequent short hacking, unproductive cough was noted. On March 7, the eighth day after admission, a definite dulness on percussion was noted at the right base, in the axillary line, and numerous constant, fine crepitant râles were heard. The heart rate remained regular and the pulse rate was 120, but the heart sounds were of poor quality. The temperature was between 103 F. (39.4 C.) and 104 F. (40. C.). The cough persisted and continued to remain unproductive.

Two days later, although her condition appeared unchanged, the consolidation involved the entire right lower and middle lobes. The breath sounds were distant, and the breath for the first time was noted to have a foul sweetish odor. A diagnosis of right pulmonary gangrene was made and a roentgenogram was taken.

The report of the roentgen-ray examination follows:

There was an irregular patchy consolidation scattered throughout both lungs, more pronounced in the other part of the second and third intercostal spaces on the right side. There were some areas of cavitation in the right first, second and third intercostal spaces. The process suggested pneumonia of the patchy type with numerous areas of cavitation.

On March 10th, the patient grew worse rapidly and toward evening became comatose. At 1 a. m., the following day, she vomited bloody mucus, and died an hour later.

Diphtheria cultures from the nose and throat were uniformly positive. The results of urinalyses were negative until March 8, when albumin, many pus cells and a few granular casts were reported. Practically no sputum was raised at any time.

The patient had diphtheria, which was apparently clearing up on the seventh day after onset, but death from pulmonary gangrene occurred seven days later. There was no hemoptysis until just before death. The acuteness of the process rendered antispirillar and surgical treatment impossible.

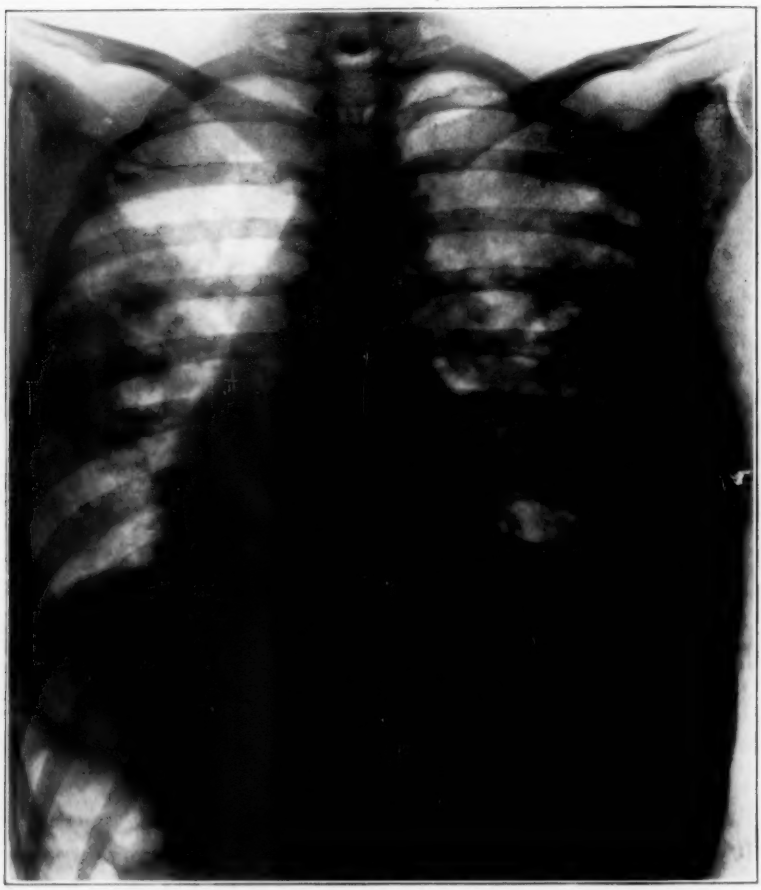
Autopsy.—Autopsy was performed twelve hours postmortem, March 11, 1927. Permission was received to examine only the lung.

The body was that of a well developed colored girl without evidence of any wasting disease, tuberculosis, syphilis or eruptions of the skin. There was a moderate cervical adenopathy. Even before the body was opened, an overpowering foul sweetish odor was noticed. As only the thorax was opened, an incision was made in the midline anteriorly.

The heart was of normal size and color and was not examined. In the left pleura, on the visceral layer, there was a mucupurulent discharge. The lung was

adherent in the costophrenic sinus, and adhesions were readily broken down. There was no free fluid. The left lung was normal on gross examination, except for the presence of pleurisy. The right pleural cavity contained a few cubic centimeters of bloody fluid, but no adhesions were found between the two layers of the pleura.

The right lung, showed a distinct line of demarcation between the practically normal upper part and the gangrenous lower two thirds. The line of demarcation



Roentgenographic appearance of pulmonary gangrene following diphtheria.

ran from the region of the third rib at its sternal attachment to about the third dorsal vertebral spine, thus being a little higher posteriorly than anteriorly. It was thought that this line rested wholly in the upper lobe, but the interlobar fissures were not defined in the gangrenous area.

Above the line of demarcation was roughly one third of the volume of the right lung. Here there was a moderate congestion, but no other abnormality. There was no discernible inflammatory or hyperemic line between the dead and the living tissue; on one side the lung was almost normal, on the other it was gangrenous; the area of transition was only about a millimeter in diameter. No

suggestion of the three zones described by Cornil and Ranvier was found. In the two thirds of the lung below the line of demarcation, the pulmonary tissue was of about normal size, but so soft that it resembled a liquid almost as much as it resembled solid material, it was uniform dark red throughout. Markings were not seen between the lobes. On section, the mass was so viscous that it scarcely held its form after being cut. Neither granular pledgets nor any suggestion of any sclerosis was found. There was no definite cavity in the lung.

Microscopic Examination.—In some of the less involved portions of the gangrenous areas, the walls of the vesicles could still be discerned. These were filled with fluid and cellular elements in which cells simulating desquamated epithelium predominated; a few polynuclear cells were also present. The vesicular walls themselves did not show any finer structures, as they were a homogeneous eosin-staining network. In some areas, the staining in the walls strongly suggested that of hemoglobin in granules; in other regions, close to the ones described, the vesicular contents were completely necrotic. In still other regions, the whole mass was amorphous and confluent without demonstrable remains of any structure. No nuclei, either epithelial or leukocytic, were seen in several contiguous fields. This area was simply a mass of mingled darker and lighter eosinophilic necrotic tissue. There was no suggestion of remaining elastic tissue.

Bacteriologic Examination.—Smear from the lung showed definite fusiform and spirillar forms, giving the typical picture of the usual Vincent's organism in considerable amount. Cultures on Loeffler's serum medium showed a heavy growth of practically pure Klebs-Loeffler bacillus, of characteristic morphology. Virulence tests were not made. Culture on 1 per cent dextrose veal broth and blood agar plates showed streptococci which did not cause homolysis, and staphylococci. Anaerobic cultures or smears for tubercle bacilli was not made.

We are unable to suggest whether or not the fusospirillar forms were of etiologic importance in this case, but we feel that the diphtheria bacilli probably were.

SUMMARY

A case of pulmonary gangrene following acute diphtheria in a previously healthy colored girl, aged 15, is reported. The symptoms were suggestive of gangrene for only forty hours before death; practically no sputum was raised. At autopsy, the lower two thirds of the right lung was completely gangrenous. Mixed flora in the lung included diphtheria bacilli, nonhemolyzing streptococci, staphylococci and Vincent's fusiform and spirillar organism.

PATENT DUCTUS ARTERIOSUS, HEMATOMA OF THE LEFT SUPRARENAL GLAND, MENINGEAL HEMORRHAGES AND DIVERTICULUM OF THE ILEUM

REPORT OF A CASE IN A CHINESE INFANT *

ANNIE V. SCOTT, M.D.
TSINAN, SHANTUNG, CHINA

The mother of W., a boy born at Shantung Christian University Hospital, had had two previous pregnancies. Both parents were Chinese. There was no family history of tuberculosis or syphilis. The mother's blood Wassermann reaction was negative. The first child died of dysentery; the second died of convulsions at about 2 months of age.

Labor began at the anticipated time, was not prolonged and ended in spontaneous delivery. The infant's measurements were: length, 51 cm; head, 35.5 cm.; thorax, 35 cm. and abdomen, 35 cm. He weighed 3,435 Gm. There was no difficulty in eliciting a vigorous cry immediately after delivery. The skin of the scalp, face, ears and neck was markedly cyanotic at birth. There was also cyanosis of the mucous membrane of the mouth. The skin of the body and limbs was also slightly cyanotic, being most marked on the forearms and legs. This cyanosis gradually decreased, until on the fourth day after birth, the skin of the body was normal. Cyanosis of the other parts decreased, but was constant until death.

Respirations were regular and full. The apex of the heart was palpated in the fifth left interspace on the nipple line, and there was slight enlargement of the heart to the right. The heart action was normal in rate, rhythm and quality. No murmur or abnormal sound was heard over the precordium. The tongue was wide and thick and constantly protruded from the mouth. The frenum extended to the tip. Other abnormal symptoms were not present.

The infant was put to the breast six hours after birth and at three hour intervals thereafter. He nursed vigorously. The mother's milk was insufficient, but the supplementary feedings were taken satisfactorily. The stools were normal. The umbilical cord was dry until it fell off. On the sixth day after birth, a yellowish discharge was noticed coming from the umbilicus. On the same day, slight jaundice of the skin of the face and body appeared. On the seventh day, this jaundice was marked, and a petechial hemorrhagic area appeared in the skin in the upper part of the left side of the chest posteriorly. During the same morning it was noticed that the infant did not nurse vigorously. By noon he could not be induced to take the breast. New abnormal observations were not evident on physical examination. At 4 p. m. of the same day, respirations and heart action became irregular. The patient soon developed evidences of failure of the right side of the heart, and he died at 9 p. m. of the same day.

The only laboratory observations of interest were the erythrocyte counts and the hemoglobin estimations.

A complete biopsy was performed, and the abnormal observations were reported by Dr. L. E. Braafladt.

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The skin and conjunctivae were slightly yellowish. The tongue was wide and thick and protruded a little. The abdomen was prominent in the epigastric region.

The skeletal muscles and all organs were tinged slightly yellow. There was a small amount of bloody fluid in the abdominal cavity. The liver was large. The vessels of the mesentery were injected, and numerous small glands were seen in it. There were adhesions about the lower pole of the spleen, the upper pole of the left kidney and the descending colon. There was a diverticulum extending from the ileum at a point 10 inches (25.4 cm.) above the cecum, 3 cm. in diameter and 5 cm. in length, through which a probe could easily be passed from the lumen of the ileum to the navel.

The heart was large, and was in firm systole. The right auricle was markedly distended, with blood clot, as were the large veins entering it. The myocardium was tinged yellow. The heart weighed 25 Gm. The foramen ovale, though not entirely closed, still covered the opening sufficiently to prevent communication between the two auricles. The aorta and the pulmonary artery were normally formed, but the ductus arteriosus was a large patent tube 3 mm. in diameter.

The lung crepitated throughout and appeared normal, except that it was markedly congested. The bronchi contained frothy, bloody fluid.

The tongue was large, wide and thick and the frenum linguae extended forward to the dental ridge of the lower maxilla.

TABLE 1.—*Erythrocyte Counts and Hemoglobin Estimations*

	Erythrocytes	Hemoglobin (Sahli)
First day after birth	8,640,000	101
Third day after birth	9,264,000	99.5
Fourth day after birth	8,320,000	102
Fifth day after birth	7,976,000	106
Sixth day after birth	8,088,000	102
Seventh day after birth	7,300,000	108.8

The left kidney appeared larger than normal. On removal, the upper half was found to consist of a hematoma 4 inches (10.1 cm.) in circumference, containing about 2 ounces of fluid blood. This portion adhered to the spleen and intestine, as has been mentioned. What appeared to be part of the suprarenal gland was still found along the lower edge of the hematoma. On making a longitudinal section through the hematoma and the kidney, it was seen that the hematoma was not of the kidney but of the suprarenal gland, the kidney itself forming what externally appeared to be the lower half. The cortex and pelvis of the kidney were normal. The wall of the hematoma was from 2 to 3 mm. thick; the inside of it had the appearance of the suprarenal medulla. The left kidney, together with the wall of the hematoma, weighed 45 Gm.

Microscopic sections of the wall of the hematoma showed that the hemorrhage was surrounded by suprarenal tissue.

In the loose tissues below the scalp were small blotches of hemorrhage along the frontal suture and the transverse sutures of the occipital bone and the lamboidal sutures. On removal of the bones of the skull and the brain, small blotches of hemorrhage, varying from 1 to 3 cm. in diameter, were found in the meninges; a few were over the hemispheres of the cerebrum, but most of them were at the base of the cerebrum. These hemorrhagic blotches were not extremely deep.

The bone marrow was dark red and appeared hyperplastic. The anatomic diagnosis was patent ductus arteriosus, hematoma of the left suprarenal gland, meningeal hemorrhages and diverticulum of the ileum.

ABSCESS OF THE BRAIN IN INFANTS UNDER TWELVE MONTHS OF AGE

A REPORT OF TWO CASES WITH SEVENTEEN COLLECTED CASES *

HEYWORTH N. SANFORD, M.D.
CHICAGO

Textbooks on pediatrics, surgery and neurology state that an abscess of the brain is extremely rare in the first decade of life. The general opinion is that an abscess of the brain rarely occurs in the young infant. Holt [1] has collected twenty-seven cases of this type of abscess which occurred in the first ten years of life; thirteen of these occurred during the first twelve months. Doyle [2] has reported one case, which will be discussed in the summary. It is doubtful whether this was a true cerebral abscess. Walter [3] has reported two cases and Dandy [4] one. The following two cases are reported in detail, while the remaining seventeen are summarized briefly.

REPORT OF CASES

CASE 1.—F. G., an infant, aged 3 months, was sent to the hospital from the dispensary on May 6, 1922, with a condition diagnosed as hydrocephalus. The child was the first born, at full term, normal delivery, and was breast fed. The mother said that she thought the child's head was large at birth, but that it did not show any great change until three weeks prior to the child's admission to the hospital. Since that time, it had grown rapidly.

Physical examination showed a well nourished child, weighing 12 pounds 6 ounces (5,712 Gm.). The temperature was 99 F., and the patient was not acutely ill. There was a marked hydrocephalus. The bitemporal measurement was 12 cm., the biparietal, 15 cm.; the occipital mental, 18 cm.; the occipital frontal, 16 cm., and the circumference, 50 cm. The superficial veins were extremely prominent; otherwise the symptoms were normal. The hemoglobin content was 80 per cent; the erythrocytes numbered 4,320,000 and the white blood cells, 16,500. The results of the urinalysis were negative.

A ventricular puncture was performed and phenolsulphonphthalein was injected; this was followed by a spinal puncture in thirty minutes. The fluid from the ventricle was straw-colored and thick. The spinal fluid was a little

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* Received for publication, Oct. 28, 1927.

* From the Department of Pediatrics, Rush Medical College of the University of Chicago, and the Presbyterian Hospital of Chicago.

1. Holt, L. E.: A Report of Five Cases of Abscess of the Brain in Infants, Together with a Summary of Twenty-Seven Collected Cases, Arch. Pediat. **15**:81 (Feb.) 1898.

2. Doyle, W. J.: Cerebral Abscess in a Child Three Months Old, New York M. J. **70**:145 (July) 1899.

3. Walter, F.: Two Cases of Abscess and Hydrocephalus in Infants, Klin. Wchnschr. **2**:2430 (Dec. 2) 1922.

4. Dandy, W. E.: Intracranial Tumors and Abscesses Causing Communicating Hydrocephalus, Ann. Surg. **82**:199 (Aug.) 1925.

cloudy, but of a clear color. Examination of this spinal fluid showed that the Wassermann reaction was negative; the Nonne-Apelt reaction was ++ and the Lange test 2344443210.

During the following week, several convulsions occurred, and the child's condition gradually grew worse. He refused to nurse or to accept artificial feeding and steadily lost in weight. The fluid obtained after a second spinal puncture contained 244 cells; the Nonne-Apelt reaction was ++ and the Lange test 2345554321.

The steady decline caused a decision for operation; this was performed on May 30. Under local anesthesia the scalp to the left of the superior sagittal sinus was incised. A corpus callosum curved trocar was introduced, the corpus was pierced, and about 3 ounces of thick green pus was obtained. The following day, the child was drowsy, and the temperature rose to 103 F. The fluid obtained at the time of operation showed diplococci in groups, which on culture were found to be staphylococci.

From this time on, the child began to vomit projectally and to have two or three convulsions daily. The brain gradually herniated through the wound, the hernia attaining the size of a walnut. Death occurred on June 17.

Autopsy showed multiple abscesses of the brain with a jelly-like mass of abscess formation over the entire left hemisphere. There were two small abscesses of the median lobe, which had a pyogenic membrane. There were also two abscesses in the right hemisphere—one below the superior frontal gyrus which had a pyogenic membrane, and another superior to the lateral ventricle. There was not any evidence of an infective process in the internal auditory canal or spinal cord. The umbilical vessels and the bones were normal. There was not a sign of an infective process anywhere in the body or anything else noteworthy.

Case 2.—R. R., an infant, born at the hospital June 2, 1927, was the first child, normal delivery, born at full term, and weighed 8 pounds and 12 ounces (3,968.9 Gm.). He was breast fed, and weighed 8 pounds and 10 ounces (3,912.2 Gm.) on his discharge from the hospital on June 12. The blood at birth showed: hemoglobin, 106 per cent; erythrocytes, 5,180,000, and white blood cells, 13,200. The results of the urinalysis were negative.

On July 19, the mother brought the child back to the hospital, saying that the day before he had had three convulsions, which were accompanied by the "twitchings of his arms and the rolling of his eyes back in his head." He had been well until that time, except for a paronychia of the right thumb and a slight serous discharge from the umbilicus, both of which had healed spontaneously.

Physical examination showed a well nourished child, weighing 12 pounds and 10 ounces (9,879.3 Gm.). The temperature was normal. At the time of examination, jerking movements of the left arm, twitching of the left lip, and blinking of the right eye were noted. The results of the examination were otherwise negative, except for a left ankle clonus. The blood showed: hemoglobin, 90 per cent; erythrocytes, 4,100,000, and white blood cells, 14,500; of these, 67 per cent were neutrophils, 30 per cent small lymphocytes, 2 per cent large lymphocytes and 1 per cent transitionals. The blood calcium was 9.82 and the Wassermann reaction was negative. The results of the Pirquet test and urinalysis were also negative. The spinal fluid was blood-stained; this staining evidently occurred during the puncture. The fluid contained 140 leukocytes and 130 erythrocytes and gave a positive Nonne-Apelt reaction. Four days later another puncture was performed; the result of the Lange test was 1122100000. There was no increase in pressure.

Following the last spinal puncture, the child's temperature rose to 103 F., but it dropped to normal. He remained in the hospital until July 30. At the time of discharge, he appeared to be much improved and had gained 4 ounces in weight. The twitchings had entirely disappeared, but the ankle clonus was still present to a slight extent on the left side. The diagnosis on discharge was encephalitis.

On August 2, the mother brought the child back to the hospital, saying that he had been well until three hours before, when, while nursing, he had suddenly stiffened and had had a convulsion. He refused to nurse, and had continued to twitch as he had done three weeks before.

Physical examination showed a well nourished child, aged 2 months, weighing 12 pounds and 14 ounces (5,838 Gm.). The temperature was 98 F. The results of examination were again negative, except an internal strabismus of the left eye and a slight left ankle clonus were noted. Examination of the blood revealed: hemoglobin, 78 per cent; erythrocytes, 4,000,000, and white blood cells, 19,650, of which 40 per cent were neutrophils and 60 per cent small lymphocytes. The spinal puncture again resulted in a bloody fluid.

From this time until August 15, his condition grew gradually worse. The temperature rose daily to 101 F. at 4 p. m., and then dropped to 99 F. The patient did not lose weight, although he was entirely breast fed. Each day he would have one or two, three minute convulsions, consisting of a slight stiffening, followed by twitching.

On August 15, another spinal puncture was performed, and a thick yellowish-green fluid was obtained under increased pressure. Following the usual procedure, with a cloudy fluid, 15 cc. of antimeningococcic serum was given the patient. The spinal fluid contained 7,500 cells, most of which were neutrophils. The Nonne-Apelt reaction was highly positive, and the Lange test was 0011123210. There were a number of gram-positive cocci in groups, with marked phagocytosis. Cultures gave an abundant growth of *Staphylococcus aureus,* which were slightly hemolytic.

Three days later, in a dosage of five billion autogenous vaccine was injected into the sinus, and blood cultures were taken. In twenty-four hours, these showed 60 colonies of staphylococcus per plate. On the following day, attempts to make spinal and cistern punctures failed. A right ventricular puncture was performed, and a yellowish fluid under pressure was obtained; it contained 17,200 cells. Fluid obtained by left ventricular puncture contained 8,000 cells. A number of staphylococci were present; but phagocytosis was not so marked. The blood count revealed 23,000 white cells, mostly polymorphonuclears.

The child's condition was growing worse. He was nursing fairly well and was not losing in weight, but he was having twitching movements of his arms, legs and face almost continuously. His temperature did not rise above 100 F. Attempts to perform spinal and cistern punctures again failed. On August 20, he was given a second injection in a dosage of five billion autogenous vaccine into the sinus, and blood cultures were again taken. In twenty-four hours these showed twenty-eight colonies of staphylococcus per field. Both ventricles were tapped again, and about the same number of cells were found in each. Only about 20 per cent of the leukocytes were motile. The child's condition grew steadily worse. He was having convulsions almost continuously, and the temperature steadily rose to 106 F., where it remained until death. A diagnosis of staphylococcic meningitis was made.

Autopsy showed an immense abscess of the right cerebral hemisphere. This abscess extended from within 1 cm. of the tip of the occipital pole forward to the level of the optic chiasma. It also extended into the frontal lobe and into

the tip of the right lateral ventricle to within 1 cm. of the frontal pole. The abscess, together with the anterior horn, occupied about four fifths of the right cerebral hemisphere. Both ventricles were dilated, and there was a diffuse meningitis. The spinal canal was blocked by a mass of fibrin, but there was not any evidence that the infection had spread up the canal. Evidence of an infective process was not found in the internal auditory canal or spinal canal. The umbilical vessels and the bones were normal. There was no sign of an infective process anywhere in the body, or anything else which was noteworthy.

SUMMARY

The case reported by Doyle is not included in this summary, as there is some doubt as to whether or not there was a true abscess of the brain in his case. The child was ill for four days with diarrhea and had a temperature of 104.5 F. He then presented a fluctuating swelling over the anterior fontanel. Doyle reports the operation as follows: "An incision one inch in length was made in the scalp extending anteroposteriorly about one fourth of an inch to the right of the median line. The scalp was firm and thickened. On puncturing the dura, it was found to be tough and resisting; on cutting forward for about one-half an inch, I was surprised to find that I had penetrated the longitudinal sinus, announced by a profuse flow of venous blood. This hemorrhage was so profuse and persistent that the wound had to be packed to check the flow, and the operation postponed. The dressing was removed forty-eight hours later. The hemorrhage had apparently ceased almost immediately. There was no pus; neither had any appeared the day previously. The wound was lightly packed with gauze. The child had rested comparatively well during the night. The temperature was 101 F., and there was no vomiting. The bowels were open, but the movements were still green.

"On the following day, when the packing was removed it was found saturated with a greenish foul discharge which welled up from the bottom of the wound; about 3 fluid drachms or one-half a fluid ounce had drained. The wound was washed out with a mercuric solution of chloride and repacked lightly in expectation of its sufficiently draining without further interference. The temperature had fallen to 99 F. The next day there was practically no pus and there has not been any since."

The child then developed a mild case of erysipelas on the head and face. From this he recovered, and was well at the time this report was written.

In a résumé of the eitology of the sixteen other cases reported with the two preceding ones, many of the factors were considered as causative. Two cases were traumatic, and one probably so (Holt); one case was due to otic involvement and four were probably due to this (Holt); two were due to infection, one following pyemia (Holt), and the other was probably due to an umbilical infection or paronychia

(Sanford); one was due to a spina bifida (Holt); one was due to a birth injury (Dandy), and in six the cause was unknown. This, therefore, gives as a cause: trauma, 16 per cent; otitis, 31 per cent; infection, 10 per cent, spina bifida, 5 per cent, birth injury, 5 per cent, and an unknown cause, 33 per cent.

Morbid Anatomy.—The abscess was located in the cerebellum in four cases, or 22 per cent (Holt), and in fourteen cases in the cerebrum, or 78 per cent. The cerebral abscesses were multiple in six cases, or 43 per cent (Holt, Dandy and Sanford). In the single abscesses, five or 36 per cent were located in the frontal lobes; three in the right lobe and three in the left. One abscess, or 7 per cent, occurred in the left parietal lobe (Holt). Two abscesses, or 14 per cent, occurred in the temporal lobe; one, in the left lobe (Holt) and one, at the tip of both frontal lobes (Dandy).

Cultures were made in ten of the cases. In one of these, or 10 per cent, the organisms was not identified (Dandy). In the nine other cases, or 90 per cent (Holt, Walter and Sanford), it was found to be staphylococcus.

Symptoms.—The general physical condition of the infants was good in sixteen cases, or 89 per cent, and poor in two cases, or 11 per cent. The temperature was normal in four cases, or 22 per cent, and irregular in fourteen cases, or 78 per cent. However, all eighteen patients showed a high terminal temperature.

All of the patients showed definite cerebral symptoms of some sort. Eighteen patients, or 100 per cent, had convulsions at some stage of the disease; the other symptoms were varied. Three patients, or 20 per cent, showed rigidity of the extremities; two, or 13 per cent, had Kernig's sign; one, or 6.5 per cent, had exaggerated knee jerks; one or 6.5 per cent, had ankle clonus, four or 27 per cent, vomited and four or 27 per cent, had opisthotonos. Three patients did not have cerebral symptoms given.

Thirteen patients, or 72 per cent, showed symptoms of the eyes; of these, five, or 38 per cent, had nystagmus, five, or 38 per cent, had internal strabismus, and three, or 24 per cent, had dilated pupils. In five cases, or 22 per cent, the condition was definitely hydrocephalus (Holt, Dandy, Walter and Sanford).

An examination of the spinal fluid was made in thirteen cases; an increased number of cells was found in all. The minimum number of cells found were 100 and the maximum 7,500. Cultures were made in ten of these cases, or 100 per cent, all of which were positive (Holt, Dandy, Walter and Sanford). A Nonne-Apelt test was made on seven spinal fluids, and there was a positive reaction seven times, or 100 per cent. A Lange test was made twice, and a strong reaction was found in the tubes three to nine in both cases, or 100 per cent (Sanford).

Diagnosis.—The diagnosis was made at the time of operation on two occasions, or 11 per cent (Walter and Sanford), and at autopsy on the remainder, or 89 per cent. The differential diagnosis appears to be between meningitis and tumor of the brain. Fifteen cases, or 84 per cent, were diagnosed before death as meningitis; one case had previously been diagnosed as encephalitis. This was due to the cerebral symptoms, cell count over 100 and organisms in the culture. Three cases, or 16 per cent were diagnosed as tumor of the brain (Dandy, Walter and Sanford). This was due to cerebral symptoms, hydrocephalus and cell count of 100 cells or slightly over. It is interesting to note that cultures were not made until after operation.

Course.—The maximum duration of the disease was fourteen weeks (Walter), and the minimum duration was six days (Holt). The general average was six weeks.

Prognosis.—Disregarding Doyle's case, the mortality was 100 per cent; all the patients died.

Treatment.—Three patients, or 16.5 per cent, were treated medicinally for meningitis. One received autogenous vaccine and two antimeningococcic vaccine (Walter and Sanford). All of the patients died. Operation was performed in four cases, or 22 per cent (Dandy, Walter and Sanford); all of the patients died. Doyle's case is again excluded, although, if the condition was a true cerebral abscess, the patient recovered following operation.

CONCLUSIONS

1. Abscess of the brain must be considered when an infant has bizarre cerebral symptoms, accompanied by a spinal fluid showing an increased number of cells and a culture of pyogenic organisms (staphylococcus).

2. Prompt recognition of this condition, with surgical drainage, might result in a lowering of the 100 per cent mortality.

30 North Michigan Boulevard.

Progress in Pediatrics

THE FATE AND DEVELOPMENT OF THE IMMATURE AND OF THE PREMATURE CHILD

A CLINICAL STUDY

Review of the Literature and Study of Cerebral Hemorrhage in the New-Born Infant *

AARON CAPPER, M.D.
Assistant Demonstrator, Department of Pediatrics, Jefferson Medical College
PHILADELPHIA

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INTRODUCTION

PART I

The purpose of the present study is twofold: (1) an investigation into the immediate and mediate causes of death of the immature infant and (2) a determination of its ultimate growth and development. The question as to the fate of immature new-born infants and their physical

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* The Corinna Borden Keen Research Fellowship Essay of the Jefferson Medical College. From the Children's Clinic of the University of Vienna, Prof. Clemens Pirquet, Chief.

and mental development is a subject of practical importance; it should be of interest not only to the pediatrician and obstetrician, but also to the eugenist, child welfare worker and even to the national economist. The idea that most immature infants died from debilitas vitae or because their organs were not sufficiently developed for independent function originated with Bumm, an obstetrician, and this idea was accepted by pediatricians without further analysis. This blind acceptance was the reason for the little interest manifested in the question of the immature infant. While progress was being made in all branches of medicine and the mortality rates were being cut down in all age groups, the statistics still disclosed a colossal death rate among immature and premature infants. After discounting stillbirths due to placenta praevia, syphilis, eclampsia, contracted pelvis, premature separation of the placenta, difficult presentations and asphyxia due to pressure of the cord around the neck, there were still many cases of stillbirths or death immediately after birth for which a cause could not be found. The mother was healthy, the pelvis proportionately developed and sufficiently large, the delivery proceeded normally and the baby was not too large; in fact, in the majority of cases the baby was premature and hence very small; the best conditions possible were present for the delivery of a live baby, and yet the baby was either stillborn or died soon after delivery. It was this large number of cases that usually was classified under the diagnosis of debilitas vitae, and a further attempt was not made to analyze the problem more deeply.

Arvo Ylppö rendered a great service in the study of this subject when he published his first work on the problem in 1919. He stimulated an unusual interest in this field, and since his momentous publication there have been several other valuable contributions. Ylppö carried his studies on the growth and development of the immature infant up to the early school age, i. e., up to the eighth year. In a recent publication, M. Comberg considered the growth and development of the immature infant up to the seventh year. My study is devoted to a clinical investigation of the immature infant to a much later age, namely, up to 14.5 years, and in two cases even up to 17 and 19.5 years, respectively. My observations extend, therefore, to the late school age or to the period of puberty and in some cases to the period of occupational apprenticeship. It is hoped that the present work will throw more light on the later fate of the immature infant, and thereby help to fill an evident gap in the present knowledge of the subject.

The method involved in the preparation of this work was laborious. At first it was necessary to peruse all the histories of cases (a total of 23,016) in the Children's Clinic at the University of Vienna since its foundation, October, 1911, until December, 1926. Six hundred and thirteen, or 2.66 per cent, were selected from these as the histories of the

immature infants. After verification of the weights at birth in the various maternity departments, only 437 histories remained available. Of these, 190 children, or 43.5 per cent, died in the hospital; twenty-three others died at home after discharge from the hospital, making a total of 213, or 48.7 per cent, dead at the time of the investigation. The addresses of the remaining 224 children were sent to the police department for verification and correction; sixty-six, or about 30 per cent, moved out of Vienna into other countries, the parents died, or they could not be located otherwise. Postal cards with prepaid answers were sent to each of the 158 parents, inviting them to bring their children to the hospital for reexamination, and if impossible to do so, to reply as to the present status of the child. Thirty-eight did not respond, but forty replied, giving either the present status of the child (seventeen) or the date and cause of the child's death (twenty-three cases). One hundred and three children reported for reexamination. The total number of patients with whose fate I am therefore acquainted is 103 (came for reexamination) plus forty (replied by letter) plus 190 (died in hospital), or 333 cases, or 76.2 per cent. The fate is known of 120 of the living patients, (103 plus seventeen) of 224, or 53.6 per cent. Ylppö said that in his cases, the percentage of children reached for reexamination dropped between the ages of from 3 to 7 from 94.4 to 71.3 per cent. One hundred and three, out of 224 presumably alive, or 40 per cent, actually reported for reexaminations. M. Comberg found that in her patients between the age of from 3 to 7, fifty of ninety-seven, or 51.5 per cent, reported for reexamination.

SIGNIFICANCE OF THE TERM "IMMATURE INFANT"

In the German pediatric literature the term "premature infant" is gradually assuming more and more a clinical and less an obstetric significance. In obstetrics, a mature infant is one born at term, i. e., at the end of from 270 to 290 days, irrespective of the degree of the development of the baby. A baby born at the end of 280 days who weighs only 2,000 Gm. (over 4 pounds) is not a premature infant; on the other hand, an infant born at the end of 240 days and weighing 3,500 Gm. (over 7 pounds) is still termed a premature infant. That this is erroneous is known by the fact that the length of the duration of pregnancy is a highly variable factor, and that many babies, although carried to term, weigh less than 2,500 Gm. (5 pounds) and are less than 40 cm. long, in other words, full term babies with the weight and length of a premature infant. On the other hand, I know of many premature infants, i. e., infants born at the end of the seventh and more at the end of the eighth month, who weigh from 3,000 to 3,500 Gm. (from 6 to 7 pounds) and are 50 cm. long, in other words, premature infants with

the weight and length of full term or mature infants. This can be proved by studying Zangmeister's table, which shows the great variations in the length of pregnancy on the one hand and in the weights on the other hand.

This table shows that while most infants born between 270 and 290 days of pregnancy weigh between 3,000 and 3,500 Gm., nevertheless a fairly large number of babies weighing less than 2,500 Gm. are also born during this period. This led Ylppö to propose the term "immature" to designate any infant who weighed less than 2,500 Gm. at birth

TABLE 1.—*Zangmeister Table Showing Relation of Length of Pregnancy to Weight of the Infant*

No. of Days After Last Menstrual Period	2000-2249 Gm.	2250-2499 Gm.	2500-2749 Gm.	2750-2999 Gm.	3000-3249 Gm.	3250-3499 Gm.	3500-3749 Gm.	3750-3999 Gm.	4000-4249 Gm.	4250-4499 Gm.	4500-4749 Gm.	4750-4999 Gm.	5000-5249 Gm.	5250-5499 Gm.	5500-5750 Gm.	Total No. of Cases
150-160	...	...	1	...	...	...	...	1	...	...	...	...	...	...	...	2
161-170	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	0
171-180	...	...	1	...	1	...	...	...	...	...	...	...	...	...	...	2
181-190	...	...	1	1	...	...	...	...	...	...	A	...	...	...	...	2
191-200	...	1	...	1	...	...	1	...	...	...	...	...	...	...	...	3
201-210	...	...	1	2	1	...	1	...	...	...	...	...	...	...	...	5
211-220	1	1	2	...	3	...	...	...	...	...	...	...	...	...	...	5
221-230	2	2	6	1	3	2	1	1	...	...	...	1	...	...	...	15
231-240	5	8	17	5	5	2	2	2	1	...	...	...	...	...	...	36
241-250	4	15	31	11	16	8	8	3	1	1	...	...	...	...	...	84
251-260	9	15	50	49	45	21	13	7	5	1	1	...	...	...	...	197
261-270	6	17	69	81	100	64	37	15	4	...	3	...	1	...	...	376
271-280	5	18	44	114	191	198	131	51	17	6	4	1	...	1	B	805
281-290	6	15	10	104	168	183	153	71	31	15	2	2	1	...	...	797
291-300	2	6	11	46	82	79	81	38	22	11	2	1	...	...	1	381
301-310	2	4	7	19	32	31	32	11	10	...	...	...	...	...	...	154
311-320	...	2	3	4	17	11	9	10	1	2	1	...	...	...	...	63
321-330	1	1	1	2	8	12	7	4	4	...	...	...	...	...	...	43
331-340	...	...	1	4	4	6	1	...	...	...	1	1	...	...	...	17
341-350	...	...	...	1	1	...	3	...	...	...	...	...	...	...	...	7
351-360	...	...	...	3	1	1	...	2	1	...	...	...	...	...	...	8
361-370	...	...	...	1	1	1	A	...	...	...	...	...	...	...	...	3
Total No. of Cases	43	105	256	449	679	619	480	216	97	36	15	6	2	1	2	3006

A indicates past term babies with normal weight; B, abnormally large and heavy babies delivered after a normal term of pregnancy.

irrespective of the length of the duration of pregnancy. Twins weighing less than 2,500 Gm. at birth are also included in this group. The term "immature" infant is proposed as signifying a specific condition, namely, any infant, whether a single or a multiple birth, born prematurely, at term or even past term, whose weight at birth is below 2,500 Gm. (5.5 pounds) is an immature infant. It implies that the infant is not completely developed and is not prepared for a normal independent extra-uterine life. It means that if it had been possible for the infant to remain longer in the uterine cavity, it would have become sufficiently strong and its organs sufficiently developed for normal function. It is not untrue that the larger number of the immature infants so classified will also be premature infants; nevertheless a

considerable number will also be full term and in some cases even past term babies. Thus, of the 437 immature infants studied at the children's clinic, the duration of pregnancy could not be stated definitely in fifty-six cases; 276, or over 72 per cent, were born prematurely; 103, or over 27 per cent, were full term infants, and two were even past term (each weighing 1,800 and 2,300 Gm. at birth).

That the term "immature" as signifying a specific condition in the new-born infant with a birth weight below 2,500 Gm. is correct, is evident to all who have had to deal with new-born infants. The stigmas of the immature infant are definite and characteristic. The "immature" infants are known for their thermolability, i. e., inability to regulate and maintain their own body temperature. This is explained as being the result of the thin and almost transparent skin, and the absence of subcutaneous deposits of fat associated with an extensive vascularization. This, together with the relatively large body surface in comparison to the small body weight, leads to an excessive loss of heat through the skin. Also, the physiologic loss of weight during the first few days of life brings with it a dehydration and a consequent loss of heat. Another reason usually given for the meager thermoregulating capacity of the immature infant is the incomplete development of the heat-regulating center. Ylppö said that in the cases in which sudden extreme changes in temperature occur, the question of intracranial injuries should also be considered. One is struck by the fact that in immature infants pneumonia and other infections often run their course without a marked rise in temperature, and conversely, that high temperatures are often present without a discoverable cause for them. Considering these facts, one can understand what Massay meant when he spoke of the "regular anarchy" of the heat-regulating system in these infants as the cause of this thermolability.

I believe, in accordance with Ylppö, that the stigma of immaturity, usually given in textbooks has been found to be incorrect, that is, that the nails are only partially developed and do not reach the finger tips. Many of our immature infants had sufficiently long nails to reach, and in some cases, even to project beyond the finger tips.

The elastic tissue is one of the last in the body to reach complete development. Hence the flabbiness of the external ears, which hang like flaps of skin, is a characteristic occurrence in immature infants. The relationship that this bears to later malformations of the external auricle will be discussed in another connection.

The thick lanugo hair covering the face and body of the immature infant is well known to everybody.

A striking feature of the immature infant is the exophthalmos. It is a characteristic which becomes more prominent as the infant grows, and it lends to it an almost pathognomonic stamp. This phenomenon

disappears in most cases toward the end of the second year, but it may persist to a later age and sometimes even to adult life. Among the 103 patients who presented themselves for reexamination, my co-workers and I found definite exophthalmos occurring after the second year of life in four children; three boys aged 4 years and 9 months, 11 years and 8 months, and 12½ years, respectively, and one girl, aged 14 years. The internist should, therefore, add one more possibility to his list of causes of bilateral exophthalmos in adult life.

Another distinguishing characteristic of immaturity is the disproportionately large head. This may not be so outstanding at birth, but it becomes more striking after the second month and continues to enlarge until about the eighth month. At this period, the small infant with a large round head and bulging eyes makes such a characteristic impression on the observer, the so-called baby doll face, that the diagnosis of immaturity could at once be made. Until recently it was believed that this large head was hydrocephalic. Postmortem examinations have disclosed, however, that hydrocephalus is not present, but merely a large brain. Ylppö examined the brains of two immature infants and did not find any abnormal amount of fluid in them. He therefore proposed the term "megacephalus" instead of hydrocephalus, because the large head is due to substance of the brain and not to any abnormal dilatation of the ventricles or an abnormal accumulation of spinal fluid. The conception of the megacephalus of the immature infant is credited to Ylppö, who explained it by saying that the brain continues to grow independently of the rest of the body and reaches its normal size, but due to slow growth and development of the body, the head seems disproportionately large; in other words, the head is normal, but the body is subnormal in size. This theory is substantiated by the fact that between the eighth month and the second year, when the brain ceases its active growth, the disproportion between the head and the remainder of the body disappears, not through a decrease in the size of the head, for the measurements of the skull remain practically stationary, but through a rapid growth of the body. That the increase in the size of the head is at first due to growth of the brain is seen by the ever widening sutures and gaping fontaneles during the first six months of life, because the skull bones are not keeping pace in growth with the brain, but after the first year the fontaneles begin to decrease and the sutures to close, because the brain has ceased its active growth.

Rosenstern found that the smaller the weight of the immature infant at birth, the more frequent is the megacephaly.

Finally, the question arises as to whether or not the megacephaly of the immature infant is not due to a rachitic cerebral hypertrophy, for, as will be seen later, early rachitic changes occur almost constantly in immature infants. This possibility can be denied for several reasons.

In the first place, the rachitic cerebral hypertrophy never reaches the dimensions that the megacephaly does; in the second place, although rachitic cerebral hypertrophy appears earlier in the immature than in the mature infant, it is never seen as early as the megacephaly. Finally, the megacephaly due to immaturity does not respond to the therapeutic measures to which the rachitic hypertrophy does. It is possible, however, that the megacephaly of the later months is a summation of the effects of immaturity as well as of rickets.

IMMATURITY AND THE NUMBER OF PREGNANCIES

That the number of pregnancies seems to have a definite relationship to, if not influence on, the frequency of immature births, can be seen from the figures. In forty-nine of 437 cases the number of the gravidity

TABLE 2.—*Relation of Number of Gravidity to Frequency of Immature Births*

Number of Gravidity	Number of Cases
First	203
Second	80
Third	43
Fourth	22
Fifth	16
Sixth	9
Seventh	5
Eighth	3
Ninth	0
Tenth	1
Eleventh	2
Twelfth	1
Thirteenth	0
Fourteenth	2
Fifteenth	1
Not mentioned	49
Total	437

was not mentioned; 203 of the remaining 388 immature infants, 52 per cent, or over one half, were first born children; eighty, or about 21 per cent, were the second born and forty-three, or over 11 per cent, were the third born. In other words, as table 2 shows, there is a definite and almost proportionate decrease in the number of immature births with an increase in the number of pregnancies, or, more mathematically expressed, the probability of an immature birth is inversely proportional to the number of the gravidity.

IMMATURITY AND SEX

There seems to be little difference in the relative frequency of immature boys and girls. In 437 cases, there were 193, or 44 per cent, boys, and 244, or 56 per cent, girls. This difference is greater when one considers only the war period and the first three years following it, i. e., from 1915 to 1921, inclusive. The observation has repeatedly been made that during and immediately after a war, more boys are born

among the warring nations than girls. This has been true in Germany, Austria and Hungary during the last war. During 1915 to 1921, inclusive, 196 immature infants were admitted to the clinic; eighty-seven, or 44 per cent, were boys and 109, or 56 per cent, girls, a difference of 12 per cent. This apparent difference is really greater, when one considers that more boys were born during those years than girls. We may say, therefore, that in our cases there were more girls than boys among the immature infants. Whether this difference is universal or not, I cannot say, as the figures published hitherto were limited to premature and not to immature children.

FREQUENCY OF IMMATURITY

In view of the specific conception of the idea of immaturity, i. e., any infant whose weight at birth is under 2,500 Gm., I cannot utilize for comparative purposes the statistics hitherto published, as those data refer only to infants who were born before term.

Ylppö said that in 10 per cent of all births in Germany the infants are immature. Brandt's figures (Säuglings Krankenhaus, Barmen, Germany) show 5,439 new-born infants, of which 566, or 10 per cent, are premature. Pinard, Hahn and Francois give the percentage of immature infants in Paris as 15.4 per cent. This makes the problem of the immature infant a more vital one, since it forms such a large percentage of the births, and more especially because it is one of the principal factors influencing the neonatal death rate.

ETIOLOGY OF IMMATURITY

The patients at the clinic, arranged according to the years in which they were born (table 3), demonstrate the fact that after 1919 there has been an increase, relative as well as absolute, in the birth of immature infants. Israel and Kemkes, who reported on the immature infants from the University clinic at Frankfurt on the Main, found that their largest numbers were also born in the years 1919 to 1921. They saw therein evidence for the assertion that after the war the number of infants underweight at birth had increased in number. Bondi found that in Vienna also there had been an increase in infants with subnormal birth weight during and after the war. However true this may be, the increase in the birth of immature infants does not stop at 1921, but continues to 1925, years in which the postbellum effects are supposedly remote.

In the large majority of cases, the cause of the immaturity cannot be determined, even though the majority of the infants are also premature (72 per cent in our series). Multiple births, and especially births of twins, play a great rôle in swelling the number of immature infants. Ylppö says that from one fifth to one third of the immature infants are

twins. Schapiro reports one twin birth of every seventy-seven births, or 1.3 per cent twin births for Germany. In America, there were 1.16 per cent twin births in 1923 and 1.13 per cent in 1924. In America, in 1923, there was one set of triplets for every 10,014 children born, and in 1924, one for every 8,543 births. In Germany, triplets are born for every 7,185 births. Among our series of 437 cases, there were sixty-three, or 14.4 per cent, twins, and four, or about 1 per cent, triplets.

TABLE 3.—*Immature Infants from the Children's Clinic, University of Vienna, Arranged According to the Years of Birth*

Year of Birth	Absolute Number	Percentage
1907–1911	15	3.4
1912	10	2.3
1913	11	2.5
1914	16	3.7
1915	12	2.7
1916	17	3.9
1917	23	5.3
1918	22	5.0
1919	23	5.3
1920	44	10.0
1921	56	12.8
1922	49	11.2
1923	44	10.0
1924	50	11.4
1925	45	10.3
Total	437	99.8

TABLE 4.—*Causes of Immaturity*

	Cause	Absolute Number of Cases	Percentage
1.	Twins	62	14.0
	Triplets	4	1.0
2.	Chronic diseases of mother (tuberculosis, 24 cases; anemia, nephritis and heart disease 10 cases)	34	8.0
3.	Syphilis	13	3.0
4.	Acute diseases of mother (pneumonia, pyelitis, grip, typhoid fever)	7	1.6
5.	Habitual premature labor or familial immature births	18	4.1
6.	Gynecologic conditions (placenta praevia, "bleeding")	15	3.4
7.	Eclampsia	6	1.3
8.	Artificial induction of labor	7	1.6
9.	Trauma	8	2.0
10.	Unknown causes	263	60.0
	Total	437	100.0

In studying table 4, one can see that the etiology of the immaturity could not be determined in by far the largest number of cases. In spite of careful questioning of the mothers and painstaking study of the obstetric histories of the patients, the number of cases in which the etiology of the immaturity is unknown is 263, or 60 per cent. Ylppö could not find any cause for the immaturity in 55.2 per cent of his cases. Israel and Kemkes, from the clinic at Frankfurt on the Main, gave 76.9 per cent as the number of cases of immaturity without any known cause. Roemheld said that the cause of 58 per cent of the cases of abortus is retroversion or retroflexion of the uterus, to which Ylppö

commented that it was possible that these uterine displacements may also lead to early induction of labor in the later months of pregnancy.

I particularly desire to emphasize the small rôle that syphilis plays in the production of immaturity. Hitherto it has been taught in textbooks that syphilis is one of the principal etiologic factors in causing an immature or premature birth. Our figures and those from other clinics absolutely disprove this assumption. Among the 437 cases, there were only thirteen cases, or 3 per cent, in which syphilis could be assumed to be an etiologic factor. This observation is based on the examination of the mother's blood or of the infant's blood or on a study of the microscopic changes in the material at postmortem examination. Forty-one patients were suspected of having syphilis, and in only seven of them was the Wassermann reaction positive. Postmortem examinations were made on 151 immature infants, and in only five cases, or 3.3 per cent, were microscopic changes present which indicated syphilitic infection. In Israel and Kemkes' figures of the Frankfurt on the Main Clinic, I find that syphilis was the cause of the immature birth in 2.7 per cent of the cases in the years 1914 to 1919, and in 4.8 per cent during 1919 to 1926, the postwar period. The French statistics mention syphilis as a cause of premature birth in from 10 to 12 per cent of the cases, while in his Berlin material Ylppö found syphilis as a cause of immature birth in 3.9 per cent of the cases. Cook (America) found syphilis to be the cause of premature (not immature) births in five of seventy-seven cases, or in 6.5 per cent. The old teaching to suspect every immature or premature birth as having a syphilitic cause, is therefore erroneous, and it is not corroborated by statistical, serologic or microscopic studies.

MORTALITY OF THE IMMATURE INFANT

In view of the fact that the weight of the infant at birth has been designated as the criterion of immaturity, I think that it is valuable to investigate the lowest weight limits of viability. According to Finkelstein, the viability of premature infants begins at about a weight of from 1,200 to 1,500 Gm. at the age of from 27 to 28 fetal weeks, and a chest circumference of from 22.5 to 23 cm. Reiche said that infants with a chest circumference under 21 cm. are not viable and that those under 23 have a doubtful viability. The following cases will testify that these statements are incorrect. Galopin recorded a case—one of quintets—in which the infant weighed 320 Gm. at birth and moved its extremities; but it lived only a few minutes. Ylppö saw infants who weighed at birth between 450 and 500 Gm. who moved their extremities and cried; in one of his cases, the infant weighed 620 Gm., was 27 cm. long and lived thirty hours. Budin and Maygrier reported a case in which an infant weighing 650 Gm. lived almost one month. F. C. Davidson reported

the case of an infant who weighed 22 ounces (600 Gm.) at birth. The period of gestation was thirty-two weeks. Its length at birth was 15 inches (38 cm.). The infant weighed 1,380 Gm. at the end of one month. One of the patients at the Children's Clinic, a girl, at present aged 14, spent her first year of life in the hospital; she is said to have weighed 750 Gm. at birth, and was admitted to the hospital on the eighth day weighing 790 Gm., and on the tenth day her weight was 750 Gm. (This case was reported by Othmar Huber.) On admission, the circumference of her chest was 20 cm. and of her head 24 cm., and she was 31 cm. in length. Her fetal age was about twenty-six weeks at birth. In another one of our cases, a boy who weighed 600 Gm. at birth lived twenty-four hours. Cook reported that the youngest child to survive in his series was one whose fetal age at birth was twenty-four weeks; however, it weighed 1,740 Gm. and was 41 cm. long. Pfaundler had a patient who weighed 860 Gm. at twenty hours of age and whom he discharged from the hospital at the age of four years in good condition. These few cases suffice to show that, although the prognosis of an

TABLE 5.—*Eden's Figures on the Mortality of Premature Infants*

	Gross Mortality, Percentage	Corrected Mortality, Percentage
Hospital A (London)	41	34
Hospital B (Provinces)	41	..
Hospital C (Provinces)	46	38
Hospital D (Provinces)	30	..

infant with a birth weight under 1,000 Gm. is not good, nevertheless, a certain number of these babies can be reared, provided they are kept under continued observation in an institution for a sufficient length of time, and, what is of paramount importance, provided they can be kept free from infections.

Holt and Babbitt, in speaking of institutional mortality of new-born infants, recorded a general infant mortality of 3 per cent among 9,571 living infants; prematurity was responsible for one half of the deaths. "Prematurity, therefore," they conclude, "must be recorded as the largest single factor in infant mortality in the first 14 days of life." Eden's figures on the mortality of premature babies in England are given in table 5.

Budin's figures for Paris are: normal babies (breast fed), 17.4 per cent mortality; weakling babies (mostly premature): breast fed, 15 per cent mortality and bottle fed, 41 per cent mortality.

La Fètra reported a series of 200 premature babies at the Bellevue Hospital, of which ninety (45 per cent) died on the first day and twenty-eight on the second and third days. Only thirty of the remaining eighty-two lived to be discharged with sufficient weight and strength to be cared for at home.

Table 6 represents a comparison of the mortality of immature and premature infants (the last four groups include only immature infants) in the various clinics, arranged according to weight at birth.

All the figures presented in the table represent results of institutional care. Feilchenfeld reported the results of caring for the immature infants at home, and he concluded that infants under 1,200

TABLE 6.—*Comparison of Mortality Rate of Immature and Premature Infants from Various Clinics*

Reporters	Up to 1,000 Gm. Percentage	1,001-1,500 Gm. Percentage	1,501-2,000 Gm. Percentage	2,001-2,500 Gm. Percentage
Barmen	100	68	44.4	27.7
Crède	...	83	36	11
Budin	...	97	85.9	68.2
Betke	...	76	60	50
Maygrin	...	67.4	27	6
Bakker	...	88	34	10.5
Moll	...	36	27	18
Framm	100	69	54	39
Yippö	94	65	45	34
Schwarz and Cohen	...	77	50	36
Hamburg-Eppendorf	100	84	54	46
Frankfurt (Israel and Kemkes)	98.5	83	48	35
Brandt	100	68	44	28
Vienna (Capper)	83	55	48	30

TABLE 7.—*Mortality of Immature Infants Arranged According to Weight Groups*

	All the Cases		Under 1,000 Gm.		1,001-1,500 Gm.		1,501-2,000 Gm.		2,001-2,500 Gm.	
Died Within	No.	%	No.	%	No.	%	No.	%	No.	%
First 24 hours	21	4.8	7	38.9	8	10.3	4	2.0	2	1.4
One week	54	12.4	11	61.1	21	27.0	17	8.7	5	3.4
One month	117	26.8	14	77.7	31	39.8	46	23.5	26	18.0
Six months	185	42.3	...	....	41	52.6	88	44.9	42	29.0
One year	196	44.9	15	83.3	43	55.1	94	47.9	44	30.3
Two years	200	45.8	...	....	44	56.4	97	49.5	...	....
Three years	202	46.2	...	....	45	57.2	98	50.0	...	....
Four years	205	46.9	...	....	...	....	99	50.5	46	31.7
Five years	207	47.4	...	....	46	58.9	100	51.0	...	....
Six years	208	47.6	...	....	...	....	...	....	47	32.4
Seven years	209	47.8	...	....	...	....	101	51.7	...	....
Eight years	211	48.3	...	....	47	60.3	102	52.0	...	....
Nine years	...	....	...	....	...	....	...	....	...	....
Ten years	...	....	...	....	...	....	...	....	...	....
Eleven years	...	....	...	....	...	....	...	....	...	....
Twelve years	...	....	...	....	...	....	...	....	...	....
Thirteen years	...	....	...	....	...	....	...	....	...	....
Fourteen years	213	48.7	...	....	...	....	104	53.1	...	....
Total number	437		18		78		196		145	

Gm. must be cared for in a hospital and those from between 1,200 to 2,000 Gm. should be cared for in a hospital.

Table 7 represents the mortality of our cases arranged in birth weight groups. The figures show that of 437 immature infants, about 45 per cent were dead at the end of the first year and about 49 per cent at the end of the fourteenth year, in other words, less than a half of all immature infants die during the first year, but after that the mortality is only a little higher than in the case of mature infants. When the mor-

tality rate according to birth weight groups is studied, however, some interesting facts are discovered. About 40 per cent of the immature infants who weighed less than 1,000 Gm. at birth died within the first twenty-four hours, whereas of those weighing between 2,000 and 2,500 Gm., only about 1.5 per cent died during the first twenty-four hours. At the end of the first year, 83 per cent of all immature infants under 1,000 Gm. are dead and only 30 per cent of those weighing between 2,000 and 2,500 Gm. This indicates that the prognosis regarding the survival of an immature infant depends first and foremost on its weight at birth, and that nursing care, thermoregulation, prevention of infection and proper feeding, although important, play only a secondary rôle. The smaller the infant, the less resistance it has, not only against trauma at birth and instrumental delivery, but also against drugs, such as morphine and pituitary.

All other factors being equal, the first year is the critical one for immature infants, since almost one half of them die during this period. The ones that naturally fare the worst are those who weigh less than 1,000 Gm., their chances of survival being only about 15 per cent. The prognosis becomes better with an increase in the birth weight, and there are even chances for the infant weighing from 1,500 to 2,000 Gm., and more than two-thirds chances of survival for the infant weighing between 2,000 and 2,500 Gm.

Ylppö found that the mortality rate in his twin births was generally less than in the single births. While at the end of the first year 50 per cent of all his patients were dead, he found that in the case of twin infants only 30 per cent were dead. Of his immature children that reached the school age, there were from 40 to 45 per cent, whereas of twins alone there were 50 per cent. Ylppö based this comparatively lower mortality rate among twins on the fact that the immature birth in these cases is naturally not due to disease of the mother or of the infant, but rather to the constitutional factor. In the case of an immature birth, however, in which eclampsia, trauma or syphilis are the etiologic factors, there is more likelihood that the infant also will be affected to some extent. Logical as this may sound, our figures do not support this assumption. Of sixty-three twins, at the end of the first year thirty-six, or 57 per cent, were dead, and at the end of fourteen years, only one more was dead. Hence, while the general mortality at the end of the first year was only 45 per cent, it was 12 per cent more for twins. This becomes especially striking when it is considered that there was not a disproportionately large number of infants with a low birth weight among them. There were only two infants with low birth weights, one weighing 980 Gm. and one 1,000 Gm.; the former is dead, while the latter is now 6½ years of age. Of the possible acute or chronic diseases of the mother that may have had an especially unfavor-

able influence on the infant, such as eclampsia, nephritis, tuberculosis or syphilis, we found that syphilis was the cause of death in one twin, but that all the other mentioned diseases did not play any etiologic rôle in the mortality of the twins.

IMMATURITY AND CEREBRAL HEMORRHAGE

General Considerations.—The neonatal death rate has not been changed much during the last quarter of a century, because attention had not been focused on the principal thing. Too often the diagnosis "debilitas vitae" as a cause of death has been accepted as satisfactory. It is true that a certain number of new-born infants who died in the first days or weeks succumbed to bronchopneumonia without symptoms, atelectasis, sepsis and other infections to which they did not give a febrile response because of their inefficient thermoregulation; a still larger number of deaths remained unexplained. This was due in part to the fact that the cranium was not opened, because hemorrhage—especially cerebral—was not thought of at the time of the autopsy, and because in many cases the hemorrhages were not macroscopic, and became evident only when serial sections were made and they were studied microscopically.

In the beginning of the eighteenth century, Cruveilhier maintained that cerebral hemorrhage occurred in one third of all stillborn infants. According to Seitz, from 3 to 4 per cent of all new-born children die from irreparable trauma at birth, of which intracranial trauma is the most important. Fischer claimed that as a result of his postmortem studies he felt convinced that 10 per cent of the deaths occurring during the first month of life are due chiefly to cerebral injuries at birth. Holland said that the frequency of postpartum intracranial hemorrhage in stillbirths and neonatal deaths, according to different observers, varies between 21 and 55 per cent, the latter figure being that found by Holland. One cannot help being impressed with the importance of this subject when such an authority on these problems as Schwartz declared that the pathologic characteristics of the first month of life are completely dominated by the cerebral injuries at birth.

Classification.—Holland classified hemorrhages according to location into: (1) subdural; (2) ventricular and (3) cerebral, being located in the cerebral substance. Subdural hemorrhages are, according to him, commoner than ventricular. He further subdivides them according to the degree into: (1) slight, (2) moderate and (3) severe; according to the extent, into: (1) localized and (2) diffuse; according to cause, into: (1) traumatic and (2) asphyxial. The traumatic, he said, are usually accompanied by tentorial tears and those of the falx cerebri. He found tears in 48 per cent of stillborn infants. Schaeffer found them in 91 per cent of the cases of difficult delivery by forceps. Munro and

Eustis' classification (a modification of Warwick's classification) of intracranial hemorrhages is as follows: (1) those caused by trauma—hemorrhage caused by excessive molding of the head and overriding of the cranial bones; (2) those caused by asphyxia—hemorrhage caused by excessive cerebral venous congestion with rise of intracranial pressure; (3) those caused by fetal disease—hemorrhage having no relation to labor, but being commonly caused by hemorrhagic diseases and rarely by syphilis or other toxemias. Seitz classifies hemorrhages into: (1) supratentorial, (2) infratentorial, (3) combined, (4) lateral ventricular, (5) intracortical and (6) hemorrhage about the basal ganglions, pons and medulla.

Predisposing Causes.—Vasolability is one of the most important predisposing causes of intracranial and other forms of hemorrhage in immature infants. The blood vessels of the immature as well as of the premature infant are readily traumatized or torn. This is due, perhaps, to the lack of elastic tissue in the blood vessel walls—for the elastic tissue is the last to reach complete development—or as Ylppö said, to the lack of perivascular elastic tissue. Hemorrhages may therefore occur through rhexis, i. e., through torn vessel walls or through diapedesis, i. e., through healthy, dilated vessel walls. Spontaneous hemorrhages of the skin are not uncommon in immature infants, and they have even been seen in infants delivered by cesarean section, caused perhaps by mere uterine contractions. Ylppö utilized this readiness to bleeding as a prognostic sign; he pinched the skin, and by the extent and rapidity of the resulting hemorrhage, he judged the vasolability or stability of the infant. He found that in those cases in which the test was strongly positive, the infant usually died during the first few days from hemorrhage, and in most cases from cerebral hemorrhage.

The term "hemorrhagic diathesis," as it is used by American writers on the subject of hemorrhages in new-born infants, is erroneous. The term, as used in medicine, refers to a definite group of diseases, like purpura, hemophilia and other conditions, whereas in the case of new-born infants, the trouble lies neither in the blood itself nor in any change in the vessel walls, but in an unripeness, or vasolability. If by hemorrhagic diathesis in the new-born infant a decreased coagulability of the blood is meant, I must take exception to it, for the coagulation time of the blood of most new-born infants, especially of premature and immature infants, is normally somewhat longer than that of older children, because of the bile pigments that circulate in the blood stream. This normal prolongation, however, is not the cause of hemorrhages. Sharpe and MaClaire reported observations on 500 new-born children. The coagulation time of the blood was normal in all except one of the infants, who either had bloody spinal fluid, or who later came to operation or autopsy, when definite hemorrhages were disclosed. In the foregoing exception,

the coagulation time was ten minutes, but in four clean (nonbleeding) cases, it was from eight and one-half to eleven minutes. I also feel, therefore, that Ehrenfest's warning was justified when he said that too much stress had been laid on hemorrhagic diathesis as a cause of hemorrhage in the new-born infant.

Graham claimed that hemorrhages in new-born infants are probably the result of a deficiency in oxidation, and that similar hemorrhages can be produced by direct asphyxiation or by the administration of chloroform. Asphyxia can occur as a result of: (1) disease of the placenta or premature separation of the same, (2) prolonged interval between the birth of the head and the remainder of the body and (3) pressure on the cord. These, according to MacHaffie, can lead to cerebral venous congestion, which in turn will cause hemorrhage of the cortical and subcortical vessels and cerebral veins; the resulting hemorrhage will cause increased intracranial pressure and medullary edema, which may lead to death or asphyxia at birth.

Ibrahim explained the hemorrhagic tendency on the basis of the presence of a large number of corpuscular elements and the high viscosity of the blood due to the concentration of the blood during the first few days of life. This, associated with the low blood pressure due to the relatively weak cardiac power, makes for a system that is predisposed to hemorrhage.

Another possible predisposing cause of hemorrhage in immature infants is the incomplete architectural development of the capillary system. The comparatively young science of capilloroscopy disclosed the fact that archicapillaries are a fetal stage of the mature capillaries, and that in most normal infants the archicapillaries are not found at birth. Doxiades—who coined the term "fetalismus" to describe a persistence of cardiovascular conditions that existed before birth of the infant, and who found this "fetalismus" in many immature infants—found a persistence of the archicapillaries in most immature infants. It is, therefore, possible that this antenatal state of the capillary bed is not of sufficient strength to withstand the trauma associated with uterine contractions and passage through the birth canal; therefore rupture of the vessels with consequent hemorrhage follows.

Exciting Causes.—Holland drew the following conclusions as to the etiology of hemorrhage, based on a large amount of material examined. He said:

> Excessive strain due to general compression of the whole head and simple longitudinal compression leads to an overstretching and tearing of the tentorium cerebelli and falx cerebri, areas of greatest stress, and to the rupture of certain blood vessels. The commonest site for tears is in the tentorium at its junction with the falx. The changes in the septa are transmitted to the vein of Galen, which becomes stretched, kinked and engorged; the consequent rupture of this vein or of its tributaries results in subdural hemorrhage of greater or less extent.

A theory, first mentioned by Seitz but popularized by Schwartz, as to the mechanism of intracranial hemorrhage is the one that concerns the difference between intra-uterine and atmospheric pressure. At the moment the membranes rupture, the presenting part of the fetus closes the birth canal like a ball valve. The intra-uterine part of the fetus is still under high pressure, but the part of the fetus—usually part of the head—closing the opening is suddenly released from this pressure, an enormous difference in pressure results between the uterus and atmosphere, and the body fluids tend to be sucked into the valvelike part. This great difference in pressure continues as long as the amniotic fluid surrounds the fetus. This leads to an overfilling and finally to a tear in the vessels of the part of the head that is sucked in, and a caput succedaneum results. If the suction is strong enough, a tear of the veins that lead from the diploë to the pericranium may also result; this is then raised by the accumulated blood, and a cephalhematoma results. The veins of the brain collect to form larger vessels in the pia and these in turn in the dura. The vessels of this membrane are in communication with the diploic vessels; hence, when strong enough suction is made on the diploic vessels, a tear may result in the pial vessels. This may explain the characteristic thick jello-like layer of blood on the cortex of the brain of dead premature infants. (Ylppö found most of his hemorrhages on the cortex of the cerebrum or cerebellum.) The microscopic examination of the cortex of the brain, white substance, ganglions, pons and medulla oblongata often shows dilated vessels, and here and there small and sometimes large hemorrhages.

Ehrenfest said that as a result of molding of the head, the parietal bones override and stretch the subjacent dura mater. If this overlapping is extensive, as in mechanical dystocia, or is suddenly accomplished, as in extraction by forceps, or if the dura is abnormally fragile, as in premature infants, the strained dura may break. But subdural hemorrhages are rare in immature infants as compared to mature ones, because the skull plates are almost as soft as leather and the edges are too pliable to cause trauma, and because in the immature infant the dura is more closely adherent to the skull than in normal infants, so that it can be neither folded nor stretched very much.

Although tentorial tears are rarer in immature than in full weight infants, they occur often enough to be considered here. Beneke, the discoverer of the tentorial tears, was the first to emphasize the importance of this area of trauma through his new method of opening the skull and removing the cerebrum first, thus leaving the falx cerebri and cerebelli open for inspection. As is well known, the tentorium consists of two leaves, an upper one formed by the cerebral dura and a lower one formed by the cerebellar dura. The tears are mostly in the upper leaf and usually in the free border of the same. Compression of the

head laterally or anteroposteriorly leads to a lengthening of the same and the consequent stretching of the falx. This tension on the cerebral dura causes a pull on the longitudinal fibers of the upper leaf of the tentorium, the weakest part of the falx, and brings about a separation of these fibers; hence a hole results perpendicular to the direction of the dural fibers. The lower leaf, although thinner, is rarely torn, because it is not exposed to the same degree of tension. The tear in the tentorium, of course, results in an injury to the blood vessels and more or less hemorrhage, depending on the size of the vessels torn. Schwartz argued against the assumption of tentorial tears, and said that they are merely a separation of the leaves of the duplicated dura caused by an already otherwise brought about hemorrhage. Beneke said that the direction of the fibers of the falx and their extension to the tentorial leaves undoubtedly point to the fact that the dura prevents a too great lateral flattening of the skull or a lengthening of the head. One can, therefore, conceive how a sudden or a slow, but marked, flattening of the skull will cause rupture of the free tentorial border. The lateral compression may not be large enough to cause a shutting off or narrowing of the straight sinus, which is a prolongation of the vena magna Galeni, thus leading to a rupture of this overfilled vein, or of the smaller veins in the tela choroidea and plexus choroideus which empty into the vena magna.

Pathologic Anatomy.—Hess said that hemorrhages due to tentorial or subdural tears are rare in premature, but frequent in full term, infants. In premature infants the hemorrhages are usually subarachnoidal, pial or intraventricular, but rarely into the substance of the brain itself. This agrees with Ylppö's observations at autopsy in 103 cases. He concluded:

> Most of the hemorrhages—in immature infants—occur in the pia mater and as a result we find in the new-born that the convexity of the cerebrum and cerebellum and sometimes the base of the brain are covered with a layer of blood, red when fresh, dark and sometimes yellow when old, and in one spot or another a group of torn vessels from where the blood came. Often one finds large clots of blood in the third or in the lateral ventricles. In the brain substance itself, however, one rarely finds evidence of hemorrhage.

This is in direct contradiction to the observations of the excellent pathologist Schwartz. He performed autopsies on 110 stillborn infants, premature as well as mature, who died immediately after birth or several weeks later. He found extensive hemorrhages, pial, intracerebral and also cerebromalacia in 105 cases. Contrary to Ylppö, he said that macroscopic hemorrhages in the substance of the brain is a characteristic occurrence in premature infants; large hemorrhages in the region of the vena terminalis and vena choroidea are found frequently, especially in stillborn premature infants. In full term infants, macroscopic hemor-

rhages are more rare; on the other hand, one sees microscopic hemorrhages, stasis, hyperemia and even thrombosis in these cases. In practically all cases of stillbirths that were classified as "asphyxia" or "debilitas vitae," Schwartz found typical anatomic changes in the brain.

Another favorable location for hemorrhage is on the convex surface of the brain along the longitudinal sinus due to injury of the latter, or more frequently rupture of the smaller veins at the point of their emptying into the sinus. The intensity in these cases varies from a drop of blood to a mass that looks like a red cap covering the cortex of the brain. The latter forms are especially common in young ones, and in these also the ventricles are usually blood filled. Another area of predilection is the undersurface of the cerebellum. In such cases there is also frequently a condition of hematomyelia, usually epidural.

The smaller the weight at birth, the more frequent the hemorrhages. Ylppö found hemorrhages in 90 per cent of the infants that weighed less than 1,000 Gm. at birth; in 76 per cent of those weighing from 1,001 to 1,500 Gm.; in 35.3 per cent of those who had a birth weight from 1,501 to 2,000 Gm. and in only 26.7 per cent of those weighing from 2,001 to 2,500 Gm. Hence, I may say that there is a close relationship between the degree of the development of the immature infant and the frequency of the occurrence of cerebral hemorrhage.

Necropsy Observations.—In our cases, macroscopic cerebral hemorrhage played a comparatively small rôle as the cause of death. We have the reports of 151 autopsies performed on immature infants and children of the clinic. Over one half of them showed macroscopic evidence of hemorrhage in the gastro-intestinal tract, lungs and kidneys and subcapsular liver hematomas. In many of these, unfortunately, the skull was not opened, and hence it is not known whether hemorrhage had existed. In some of those in which the skull was opened, there was no macroscopic hemorrhage; microscopic examination, however, was not made. On the basis of the hemorrhages in the other viscera, one may assume that they were probably present in the brain in a large number of the cases. Tentorial tears were found in several cases. The other half of the autopsies were made on children ranging in age from 6 months to 14 years; pneumonia, pulmonary tuberculosis and tuberculous meningitis caused the death of the majority of them.

In 1919, Warwick found intracranial hemorrhage in 50 per cent of thirty-six postmortem examinations, and in 1921, in 40 per cent of 200 examinations. Bailey found cerebral hemorrhage in 40 of 100 postmortem examinations. Parrot, saw intracranial hemorrhage in 76 per cent of thirty-four postmortem examinations performed on stillborn infants or on infants who died during the first week. Losie found hemorrhage of the brain in 25 per cent of 274 postmortem examinations. Schwartz said that he found macroscopic effects of cerebral trauma at

birth as indicated by hemorrhage or by focal or diffuse areas of softening, in 65 per cent of infants who died during the first five months. Holland found lacerations of the tentorium cerebelli in 88 per cent (!) of the infants that had died following breech delivery. He found injuries of the "dural system" eighty-one times or in 48 per cent of 168 infants who died during or soon after delivery. Meyer and Hauch found rupture of the tentorium twenty-eight times among sixty-four stillborn infants; most of these infants were premature or were born by breech presentation or by extraction. Kowitz reported 5,989 postmortem examinations on children from the Kiel institute. Of these, 1,014, or 19.9 per cent, showed intracranial hemorrhage or traces of it. Among 1,203 stillborn infants, 25.5 per cent showed hemorrhages; hemorrhage was found in 26.6 per cent of 911 infants during the first weeks of life; in 14.7 per cent in 1,715 during the first three months; in 10 per cent of 1,607 of the last three quarters of the first year; in 9.4 per cent of 543 who died during the second year. In the first two groups, the fresh hemorrhages were of the preponderating majority; in the last three groups they were residues of old hemorrhages. According to localization, dura and cerebral sinus, 55.2 per cent; arachnoidea, 23.2 per cent; the ventricles, 11.7 per cent, and brain substance, 9.9 per cent. Among 554 autopsies on new-born infants, Deluga saw dural tears and meningeal hemorrhages 210 times; they were especially common after delivery by forceps and version, but he found them also in thirty-four normally delivered infants. Foote reported 959 sections, among which he found cerebral hemorrhage 115 times, or in 12 per cent; Framm found them thirty-two times, or in 24 per cent of 132 sections; Glatz, forty-four times, or in 45.8 per cent of ninety-six sections; Hedrèn found intracranial hemorrhages or tentorial tears sixty-five times, or in 9.3 per cent of 700 sections. Schäfer observed intracranial hemorrhages 140 times, or in 20.6 per cent, of 680 postmortem examinations. In these cases, the proportion of first born to later infants was 72 : 50. Saenger found seventy-three cases of macroscopic hemorrhage during 100 postmortem examinations, forty-eight of which were extensive. Crothers reported tentorial tears in 88 per cent (!) of premature infants delivered by forceps. Hutinel and Babonneix reported 18 per cent of trauma of the brain among premature infants. Weiss examined 507 infants under 2,500 Gm. of weight at birth. One fifth of these that came to autopsy had intracerebral and intrameningeal hemorrhages. Cruickshank found hemorrhages of all types in eighty cases, or in 65.5 per cent of 200 cases of mature and immature infants. He found thirty tentorial tears, or 12 per cent. On the other hand, Jaschke reported that of 4,066 births in his clinic, only 1 per cent of the infants (after subtracting those weighing under 2,500 Gm., only 0.22 per cent) died during delivery as a result of intracranial trauma, and only 2.6 per cent of the deaths

during the first two to six weeks of life were due to cerebral trauma at birth. What has been said regarding the frequency of cerebral hemorrhage referred in many of the cases to mature infants; it is not difficult to conceive how much more appalling the figures would be if only immature infants had been considered.

There is general agreement concerning the enormous frequency of traumatic injury of the brain at birth. Some even go as far as to maintain that in every new-born infant there is some microscopic cortical hemorrhage. Since the attention of pathologists has been directed to cerebral hemorrhage, one reads with increasing frequency concerning the presence of cerebral hemorrhage, microscopic or macroscopic in postmortem reports. How much of it is the direct or indirect cause of death? That is difficult to answer. How many of the infants later develop diseases that are secondary to these hemorrhages? That I shall attempt to answer. It may be assumed, however, that as a rule only the macroscopic hemorrhages are the cause of some stillbirths, neonatal deaths or deaths within the first month of life.

Diagnosis of Cerebral Hemorrhage.—Since not all intracranial lesions at birth cause death or even marked symptoms in the new-born infant, it stands to reason, especially in view of the foregoing postmortem figures, that cerebral trauma at birth must be of enormous frequency and that it occurs much oftener than autopsy records indicate. This is especially true in the case of immature infants. Cortical injuries are sometimes difficult to diagnose, because occasionally they do not give rise to symptoms. This is more frequently encountered in immature infants, because the cortex in those infants is relatively insensitive to stimuli. Soltman proved this by means of experiments in electrical stimulation of the cortices of newly-born dogs and rabbits, in which he noticed that there was slight, if any, response to electrical stimulation. It is only after the first months of life have passed that the normal response develops. Ylppö also observed that the pharyngeal reflex (touching the base of the tongue or the posterior pharyngeal wall with the tongue depressor and the secondary "choking" or coughing reflex) is absent in infants under 1,400 Gm. weight at birth, due to the undeveloped central nervous system. This exposes those infants to inhaling food particles, since the protecting reflex is absent. Ylppö also observed that the patellar and cremasteric reflexes in immature infants either are undeveloped or show abnormal responses; the latter change, however, may be due to cerebral hemorrhage or to trauma. It is therefore wise to consider the possibility of cerebral trauma in every new-born infant whose instinctive and physiologic functions are not developing or progressing properly.

Holland said that if an infant is too somnolent or does not sleep enough, cries too much, has apneic attacks, breathes irregularly, fails

to suckle, shows rigidity, has convulsions, palsy or twitching, especially if the infant is premature, one should suspect intracranial hemorrhage and seek to discover it.

There are all kinds of respiratory disturbances. The type of infant that usually has hemorrhage is one who is born asphyctic, has to be resuscitated at birth and then develops repeated attacks of asphyxia and cyanosis; or one who after breathing normally suddenly becomes severely asphyctic and passes from one attack into another. In the latter cases, associated aphagia, persistent singultus, yawning, and frequent vomiting usually also occur. Vomiting alone should not mislead one to diagnose hemorrhage, as it is common in immature infants. Only hemorrhages that are severe enough or near enough to cause direct or indirect pressure on the medulla will give rise to aphagia, singultus and respiratory disturbances, such as bradypnea, tachypnea or apnea, and superficial or deep breathing; often one sees superficial but slow breathing. Cheyene-Stokes respiration occurs preagonally. Most observers noted tachycardia and only rarely bradycardia.

The outstanding symptoms are the convulsions and localized twitchings; the former can be clonic, tonic or mixed. Occasionally one sees typical jacksonian attacks. In general, the severer the convulsions, the worse the prognosis, as they usually point to dural or extracerebral processes, whereas hemorrhages into the substance of the brain itself—at least the smaller ones—do not cause severe convulsions or unconsciousness. Concerning localized twitchings, the facial muscles are involved most often; trismus, risus sardonicus and oculomotor symptoms may occur. Döllinger said that when there are hemorrhages in the substance of the brain, motor phenomena or palsies do not occur. Rigidity of the neck or even opisthotonus may occur, according to Ylppö, especially in hemorrhages of the spinal cord. Priapism due to injury of the cord is rarely observed. Rigidity and spasticity of the extremities are not uncommon. Unilateral or bilateral ptosis is due to hemorrhage between the pons and chiasm at the point of the emergence of the third and sixth nerves. Nystagmus may occur. Disturbances of the levator palpebrae are recognized by the wrinkling of the forehead. Convergent or divergent strabismus is an uncertain sign, as that is often normally present up to the eighth week of life. Through abducens palsy one may sometimes get a bulbar retraction and hence an enophthalmos. Chvostek, Babinski, Oppenheim, Gordon and Trousseau signs were negative in twenty-eight immature infants under 1,800 Gm. of weight and positive in three of thirty-two infants weighing between 1,800 and 2,500 Gm. Sometimes one sees in these infants a certain type of inspiratory stridor, described by Thomas as "cerebral stridor." Sharpe and MaClaire mentioned a refusal of food by these infants with cerebral injuries, but Döllinger said that it is really a difficulty in sucking, drinking and swallowing.

Even Little has mentioned disturbances in swallowing among his early observations. All degrees of sensory disturbances may occur. Headaches, hyperesthesia and paresthesia are present and are evidenced by the rolling of the head to and fro, constant whining and the sudden cry. The ease with which these infants are frightened is, according to Döllinger, a sign of acoustic and optic irritation. Stern maintained that in 75 per cent of all new-born infants he could demonstrate the finer symptoms of trauma, such as spontaneous nystagmus, and that in premature infants even normal delivery caused severe trauma in three fifths of all cases. All of Stern's infants with spontaneous nystagmus that came to autopsy showed macroscopic evidence of cerebral trauma at birth. Herz went so far as to say that the trauma of the mastoid portion of the temporal bone occurring during birth forms a locus minoris resistentiae for the later common infections of the middle ear and mastoid in children. According to Voss, trauma of the ear at birth is characterized principally by three symptoms: (1) spontaneous nystagmus, (2) no response to caloric test and (3) slight or no response to the Bárány test. Of these three symptoms, the first one is the most important. These conclusions are based on observations in ninety-three children, twenty-eight of whom weighed under 1,800 Gm. at birth; thirty-two weighed between 1,800 and 2,500 Gm., and thirty-three were of normal weight. All of the first group showed spontaneous nystagmus; twenty-four of the second group showed it and twenty-five of the third group. In all cases, it was mostly bilateral nystagmus.

Schwartz also attributed the striate symptoms, namely, choreic and athetotic movements and tremor, to cerebral trauma at birth. The eyegrounds showed punctate hemorrhages or more rarely edema in about one half of the cases. Königstein found retinal hemorrhages in 10 per cent; Paul, in 10 per cent; Veit, in 46 per cent, and Feer, in 20 per cent of the cases. Bulging of the fontanels varies considerably and is not a reliable sign. Ylppö wants to consider the "anarchy of the temperature regulation" as a result of cerebral trauma at birth. The "Hampelmann" phenomenon, described by Heubner in scurvy, is claimed by Ylppö to be characteristic of intracranial hemorrhages in immature infants. It consists in a lightning-like raising of the arms and a twitching of the legs on striking the sternum.

Early lumbar puncture is a helpful diagnostic aid in intracranial hemorrhage; but consideration of lumbar puncture observations must not be made an iron rule in the diagnosis. Sanguineous cerebrospinal fluid is found only in the presence of free blood in the subdural space or in the ventricles, but not in hemorrhage in the substance of the brain itself, which, according to Schwartz, is the most frequent form of cerebral trauma at birth in immature infants. Furthermore, one must

be slow in making a lumbar puncture in infants who weigh very little at birth, even in the presence of definite signs of hemorrhage, as the subsequent shock may be fatal.

MacHaffie said that when infratentorial tears are present, almost pure blood is obtained by puncture; when supratentorial tears are present, there is a reddish tinge or only a slightly turbid liquid in which the blood can be demonstrated only microscopically. Roberts found that all premature infants, small full term infants and twins invariably showed marked pigmentation of the spinal fluid, while, as a general rule, the fluid of large, full term infants contained relatively little pigment. He said that this parallels the observation that premature and small term infants rarely, if ever, escape jaundice. Of 423 cases in which Roberts made examinations, he found bloody spinal fluid in sixty or 14.1 per cent. In only two was the bleeding time prolonged (eleven and thirteen minutes). Fifteen of the sixty infants, or 25 per cent, were premature, while in the whole series fifty-four, or 12.7 per cent, were premature. Of the sixty infants with a bloody spinal fluid, twelve died; eight died in the hospital within the first twelve days; of the remaining infants, who had been under observation for from two to nineteen months, only two are known to have shown disturbances due to cerebral trauma. Ullrich found bloody spinal fluid fifteen times in 100 new-born infants suspected of suffering from trauma of the brain. Three who weighed less than 2,000 Gm. at birth had bloody spinal fluid; several who were delivered by forceps had clear spinal fluid. Sharpe and MaClaire performed lumbar punctures on 500 consecutive new-born infants. The first 100 infants were from 12 to 24 hours old; four of these had bloody and five had blood-tinged fluids, or 9 per cent had bloody spinal fluids. In the second series of 100 infants, 13 per cent had bloody fluids; in the third group of 100, 10 per cent. In the fourth group of 100 infants from 24 to 48 hours old, 7 per cent had bloody spinal fluids, while in the fifth group of infants from 24 to 48 hours old, 6 per cent had bloody fluids. This gives an average of 9 per cent of bloody spinal fluids in 500 consecutively born infants, mature as well as immature.

One must be careful to differentiate bloody spinal fluid due to hemorrhage from that due to trauma of the venous plexus during the puncture. If the blood is due to trauma, the spinal fluid will at first be almost pure blood and will gradually become clearer until only a faint turbidity remains, whereas blood in the spinal fluid due to intracranial hemorrhage makes the fluid uniformly bloody. If in doubt, the puncture may be repeated one interspace higher; if the blood was due to trauma by the needle, the fluid from the second puncture will usually be clear. The normal spinal fluid pressure in new-born infants is from 3 to 5 mm. of

mercury. When the diagnosis of hemorrhage is doubtful, an increase in the spinal fluid pressure may sometimes help to make the diagnosis of cerebral trauma.

Prophylaxis and Treatment in Cerebral Hemorrhage.—In view of the fact that the cerebral cortex is poorly developed in the new-born infant, especially in the immature infant, the signs of mild hemorrhage may be few, and these cases may be overlooked. It is especially in these cases in which the hemorrhage is small that the prognosis is good if active treatment is instituted. In all cases of difficult delivery or in the birth of immature infants it is therefore necessary that the possibility of intracranial hemorrhage be kept in mind. In case of doubt, a diagnostic lumbar puncture should be undertaken.

Sharpe and MaClaire, as a result of their studies on 500 new-born infants, and particularly on the relationship between the method of delivery and the frequency of trauma at birth, conclude as follows:

> The use of the early and correctly applied forceps—especially low forceps—does not increase the danger of intracranial hemorrhage, but prolonged labor causing extreme intracranial venous stasis and especially when instruments are used as a last resort, and particularly median forceps, then the danger of intracranial hemorrhage is greatly increased.

Döllinger said that prophylaxis of trauma at birth is the duty of the obstetrician; but in the case of the immature infant, even if the obstetrician utilized the most ideal prophylaxis or watchful waiting policy, hemorrhage will nevertheless occur in many cases, because the immature infant is vasolabile, and the mere uterine contractions are sometimes sufficiently traumatizing to cause hemorrhage. Ylppö mentioned hemorrhages—not cerebral—in infants delivered by cesarean section. Browne said that in breech and face presentations hemorrhages occur ten times as often as in vertex presentations. Holland said that 88 per cent of the infants born by breech presentation who died during birth showed tentorial tears. Crothers saw tentorial tears in 88 per cent of all premature infants delivered by forceps. The question of the influence of forceps on cerebral trauma at birth is still heatedly debated; all, however, agree that the forceps is a dangerous instrument in the delivery of immature babies because the blood vessels of these infants are poor in elastic tissue or the elastic tissue is incompletely developed. Schäfer spoke of this condition as the abnormal fragility of the blood vessels.

In speaking of the prophylaxis of hemorrhage of the brain, I also want to mention the Schultze method of resuscitation of an asphyctic new-born infant. As is known, this consists in swinging the baby back and forth while holding it by its feet. This is a method that should be discarded, as in several cases in which the asphyxia was due to hemorrhage the swinging increased the hemorrhage and caused immediate

death. In immature infants, in whom the blood vessels are delicate, such swinging may cause cerebral hemorhage which did not exist before the resuscitation began.

The most important part of the active treatment in cerebral hemorrhage is therapeutic lumbar puncture. It should be repeated frequently, from every twelve to twenty-four hours, depending on the severity of the hemorrhage. But if the baby is a very small, immature infant, care must be exercised, and the general appearance of the patient must be the guide for the indication of the puncture. From 10 to 20 cc. of fluid is removed with each puncture, and the punctures are continued until the fluid comes clear. If improvement does not take place, cisterna magna and ventricular drainage may be made. Ehrenfest said that coagulants, like calcium chloride, should be given even in the cases in which the bleeding and clotting times are normal. Foote proposed that the blood clotting time be taken in all new-born infants and that intramuscular injections of blood be made in all infants in whom hemorrhage is suspected. From 20 to 30 cc. of whole blood injected intramuscularly and repeated in from twelve to twenty-four hours, or from 25 to 50 cc. injected intravenously or intraperitoneally, sometimes checks the hemorrhage. Occasionally improvement follows several subcutaneous injections of from 5 to 10 cc. of a 10 per cent sterile gelatin solution. It is important to keep these infants warm, to supply them with oxygen, to keep them quiet by means of sedatives by rectum, and to supply fluids liberally. Artificial pneumocephalus or encephalography may in some cases be tried for diagnostic as well as for therapeutic purposes.

There are three operative procedures to be considered: (1) trephining, (2) subtemporal decompression and (3) removal of the hematoma if it is accessible. Cushing was the first to perform the subtemporal decompression and to remove the hematoma. Of his first nine cases (three were bilateral), four infants became entirely well. Since the publication of his first results, he has operated on more infants with equally good success. Seitz, Simmons, Henschen, Chipault, Green, Wilcox, Towne, Faber, Grossmann, Gordon, Sloan, Doazan and Sharpe also reported operative successes.

Hemorrhage in Other Organs.—As I mentioned elsewhere, over one half of the 151 infants at the clinic who came to autopsy showed hemorrhages in the lungs, gastro-intestinal tract, spleen, under the capsule of the liver or in the skin. Ylppö also described subpleural and epicardial ecchymoses. He found subcapsular hepatic hemorrhages in 80 per cent of the immature infants under 1,000 Gm. in weight, but in only 5 per cent of those from between 2,000 to 2,500 Gm. Small hemorrhages may occur also in the parenchyma of the liver. Hemorrhages in the mucous membranes are of practically constant occurrence in the imma-

ture infants, and subcapsular and parenchymatous renal hemorrhages are frequent. In a word, hemorrhages may occur in all the organs of the body, but the hemorrhages in the skull cavity are of chief importance because of their possible immediate fatal results and because of the late secondary conditions in the central nervous system.

Conclusions.—The clinical as well as the pathologic data presented show the general agreement concerning the enormous frequency of cerebral injury at birth. Wohlwill found that cerebral trauma at birth causes a loss of human life so great that it may be considered as one of the most widely spread diseases. Next to tuberculosis, disease of the nervous system due to cerebral trauma at birth is the most widely prevalent disease from the point of view of frequency. Its mortality is one of the greatest. Schwartz said that 10 per cent of all the new-born infants who at the beginning of the delivery were viable per se died by the end of the first month as a result of cerebral trauma at birth. Pathologists are of the opinion that this great loss of human life is overwhelmingly caused by the traumatic injury of the brain at birth; all other causes—congenital syphilis, asphyxia due to cord around the neck, asphyxia through anomalies of the delivery, primary infections and malformations—are present in a small number of cases when compared with the number in which trauma is the cause. Immature and premature births, of course, form the most important contingency in this group.

(To be continued)

Pediatric Biographies

PAULUS BAGELLARDUS *

?—1492

JOHN RUHRÄH, M.D.
BALTIMORE

There are three incunabula devoted entirely to pediatrics and a fourth which contains pediatric material of extraordinary interest. The first of these is by Paulus Bagellardus ab Flumine, as his name is generally given. The date and place of his birth are not known, but he was educated at Padua, and practiced medicine there. For twenty-eight years, he taught medicine as docent and for two years as ordinarius; then he was made professor of medicine. Later he removed to Venice, but as the climate did not agree with him, he returned to Padua. He died in that city in 1492, and was buried in the Portico of Saint Anthony's.

Bagellardus entitled his book "A Little Book on the Diseases of Children," in the original Latin "Libellus de egritudinibus infantium." The first edition is dated April 21, 1472, and was printed by Bartholomäus de Valdezocchio and Martinus de Septum Arboribus. The book is inscribed to Nicolo Tron, at that time Doge of Venice.

Another Latin edition was printed in 1487 and a translation into Brescian in 1486, but this edition does not bear the name of the place of publication. In the beginning of the sixteenth century another edition appeared, but it does not contain the name of the place or the date of publication or the name of the printer. This edition is illustrated with a religious picture and contains a religious introduction of Jacobus de Benevento. In 1538, still another edition appeared, this time at Lyons, with an introduction by Master Petrus Toletus, who, by the way, was at Montpellier with Rabelais, and who is mentioned by Rabelais in his immortal work. Then Bagellardus was allowed to slumber on the shelves for nearly four centuries, until in 1925, his little book was reproduced in facsimile by Sudhoff in his "Erstlinge der Pädiatrischen Literatur." In the same year, Dr. Herbert F. Wright kindly made an English translation for me, and it was printed in "Pediatrics of the Past," with translations of the other pediatric incunabula and various later texts of similar interest.

Bagellardus, like most medical writers, owed much to those who preceded him, perhaps most to Rhazes, to whom he refers fourteen times. Avicenna follows as a close second and Hippocrates, Galen,

* Received for publication, Dec. 13, 1927.

AD ILLVSTRISSIMVM PRIN
CIPEM DOMINVM NICOLA
VM TRVNO DIGNISSIMVM.
DVCEM VENETIARVM DO
MINVM SVVM PRECIPVVM.
LIBELLVS DE EGRITVDINI
BVS INFANTIVM PER MAGI
STRVM PAVLVM BAGELLAR
DVM A FLVMINE EDITVS IN
CIPIT FOELICITER.

Vantum domui tuæ illu-
ſtriſſiẽ princeps debeã: nec
Liuii nec. Ciceronis lingua
aut eloquentia exprimere:
nec quiuis alius felici ſtilo
comprehendere poſſet. Nã
cu puto me in clarũ uirũ olim euaſiſſe dũ-
taxat beneficiis illius preclari genitoris tui
patricii honeſtiſſimi: qui me innata ſibi hu-
manitate ad medicinalẽ ſedẽ euexit in qua
octo & uiginti ſolares circulos honeſte mili
taui: Ingratitudinis nota me facile ſubitur⁊
facile intelligebam: niſi ꝑ uiribus eniterer
aliquid ſaltẽ in tãta tue felicitatis aplitudine

First page of Bagellardus.

Haliabbas, Mesuë, Isaac, Serapion and others are also cited; but it must not be concluded that Bagellardus was not an authority in his own way. He uses such expressions as "I, too, have tried this"; "I do not approve"; "I myself know from experience"; "I have also seen" and similar phrases which show that he had his own views, especially concerning treatment.

This book may be regarded as a sort of compendium of the pediatric practice of the time in which it was written. The first part of the book deals with the management of the infant during the first few months; the second is divided into twenty-two chapters, each treating of a disease. Toletus added an appendix "On Certain Diseases not Mentioned by the Author." Bagellardus considers epilepsy among other conditions, and quotes the authorities on the therapeutic value of an emerald suspended on the neck, and also of the peony root and of the ashes of a prickly pig or hedgehog. One smiles, but consider this year of our Lord 1928, with its vaunted glandular extract cures! He treats of convulsions and wakefulness; for the latter, he advises that "the curing be begun with the lighter remedies, since all things which provoke sleep are narcotic and in a certain measure stupefying." Sound advice indeed!

His advice "on internal diseases of the ears" is full of sound sense. It must be remembered that the otoscope is an invention slightly more than half a century old. He cleansed, used antiseptics, astringents, diluted alcohol and alum—not at all far from modern treatment; as to water of honey; today sugar solutions are advised on ulcerated surfaces. But let Bagellardus tell his own tale:

ON INTERNAL DISEASES OF THE EARS

Sometimes children have a few pustules inside the ears, emitting corruption and water, in which there is a severe itch, whereby children are annoyed and the nurse likewise on account of the cries from pain. And, although much is said by the authorities, yet a few tried remedies we shall set forth. The first is, take old cotton, i. e., lately carded, and place in the ears after the manner of a tent; cleanse the corruption coming from the ulcer, and again insert another clean tent. The second is, insert a tent saturated with common oil or water of honey; and if the infant happens to be relieved, let the tent be repeated until complete cure. But if the corruption still runs out, then let the above-mentioned tent saturated with water of honey and powder of iris or of myrrh or of aloe be introduced until complete cure. Another remedy is similarly efficacious for the same affection: take alum and dissolve in wine and dip in lycion and introduce it. Take also nitre and grind it with water and vinegar and introduce it. But if the infant be not relieved by these, then you may know that the fistula was produced internally and the infant will not be relieved except by change of age.

All his therapeutic measures are not so sound. For constipation, he used among other things "suppositories of mouse's excrement crushed with honey or salt or hog's lard" or "a soft injection of chicken broth or sheep's head broth." When it comes to animal therapy, he vies with

unguentū factum ex unguēto ceruſe lote cū oleo roſ. & litargiro auri mirabiliter tollit Sed breue quodam addere intendo. Q; & ſi puū ſit & minimū eſt tamen uirtutis amplū non ſolum in infantibus lactātium excoriationibus .īmo etiā in nutricibus habētibus ſciſſuram extremitatum papillarū . Quod eſt tale· ℞.farine amidi ℥.ß aque roſ. quātū ſufficit . ad inſpiſſationē & fiat linimentū .

Opuſculū de egritudinibus & remediis īfātium ac totidem capitulis cōpilatū p egregiū ac famoſiſſimū artium & medicine doctorē magiſtrum Paulum bagellardum a flumīe fœliciter explicit .

Sola miſeria caret inuidia

M.CCCC.LXXII die xxi Aprilis .

BAR VAL patauus F.F.
MAR de ſeptem arboribus prutenus.

Last page of the first edition of Bagellardus showing the printer's signature.

the modern manufacturers. The following paragraph gives his views on treatment for incontinence of urine:

> Dioscorides said that the cerebrum of a hare, ground and imbibed, corrects bed-wetters. And Fidelis said that the lung of a kid when eaten and made into a plaster restrains incontinence of urine. He also said that the bladder of a young breeding sow, when pulverized and imbibed, checks urine. Rasis said that if you remove the comb of a cock and dry it and triturate it and scatter on the bed of the bed-wetter without his knowledge, he is cured. It is known from experience that if the urine passed is thick and rough, if a syrup be made of a decoction of the flowers of nenuphar and is quaffed, immediately that urine is checked and clarified.

Limited space prevents a fuller consideration which may be found with the text, in "Pediatrics of the Past," and to which the interested reader is referred. Bagellardus' text is the first printed book on pediatrics, and pioneers in any line of human endeavor are worthy of study and consideration, for, as the Germans say: "Aller Anfang ist schwer."

News and Comment

TRACHOMA

The bulletin from the National Committee for the Prevention of Blindness calls attention to the widespread increase of blindness following all wars. One of the chief causes for the increase following the late war has been trachoma. The cause of this was recently discovered by Noguchi. There are still nineteen states and two territories in which adequate legislation or regulations for prophylactic treatment has not been made. During the last twenty years, there has been a steady drop in the incidence of blindness in this country.

INTERNATIONAL AMERICAN CHILD WELFARE INSTITUTE

The International American Child Welfare Institute was inaugurated during the past summer with headquarters at Montevideo. Its functions will comprise consultations of members and the distribution of current literature on child welfare; there are four major commissions, namely, organization and institutions; laws and regulations; statistics and results, and publications.

SPANISH CONGRESS OF PEDIATRICS

The fourth Spanish Congress of Pediatrics will be held at Valencia in 1932.

AMERICAN NATIONAL ASSOCIATION OF SOCIAL WORKERS

The fifty-fourth annual convention of the American National Association of Social Workers will open at Memphis on May 2, 1928.

DR. SCHLUTZ MEMBER OF NATIONAL ACADEMY OF MEDICINE OF BUENOS AIRES

On Nov. 10, 1927, Dr. Frederick W. Schlutz was elected to honorary membership in the National Academy of Medicine at Buenos Aires.

Abstracts from Current Literature

Pathology, Bacteriology and Biochemistry

THE EFFECT OF EXPOSURE TO THE SUN ON THE SUSCEPTIBILITY OF RACHITIC RATS TO INFECTION. ELIZABETH CHANT ROBERTSON, Canad. M. A. J. **17**:1033, 1927.

This communication is a summary of results obtained in a study of the effect of sunshine on rachitic rats as measured by their susceptibility to infection.

The organism used was one normally associated with rats.

It was found that as a result of exposure to the sun twice as many young rachitic rats survived an intraperitoneal injection of living micro-organisms as compared with a similar group of control rachitic rats kept inside.

MOORE, Omaha.

SYMPATHETIC NEUROBLASTOMA. MEUNIER, Arch. de méd. d. enf. **30**:569, 1927.

In reviewing two clinical cases reported by Volpe and Bloise with a tentative diagnosis of abdominal lymphosarcoma [abstracted in the AMERICAN JOURNAL OF DISEASES OF CHILDREN **33**:832 (May) 1927], Meunier challenges the conclusions of the authors and presents arguments to show that these unusual tumors may properly be classified as sympathetic neuroblastomas. While several observations have been recorded in American, English and German literature, none has been described in France up to 1926. Since that time, five authentic cases have been studied and considerable additional evidence gathered toward establishing these rare growths in their proper relation among malignant neoplasms. A superficial examination of these tumors reveals a structure strikingly like that of a small round cell sarcoma, particularly in the metastases, but more careful study will show that these growths spring from the medullary portion of the suprarenals. Virchow, in 1865, and Marchand, in 1891, recognized nerve fibrils in these tumors and classified them as malignant gliomas. In 1910, J. H. Wright distinguished these elements from those found in gliomas and established them among the special morbid entities. Embryologically, they represent the stage of development of the central nervous system in which the cells are not yet differentiated, and in that respect are considerably more precocious than the elements responsible for the evolution of the glioma. The neuroblastoma sympathicum, a type of neuro-ectodermic tumor, is therefore to be distinguished from lymphosarcoma, from mesodermic tumors and from gliomas. While theoretically it may arise at any point where there are sympathetic neuroblasts, as a matter of fact it always springs from the medullary substance of the suprarenals which, itself, is derived from the sympathetic nervous system. With respect to its morphologic characteristics, it may be described as a small round cell formation, the cells being rich in chromatin and poor in cytoplasm—lymphocytoids. This first impression has doubtless led to the usual diagnosis of sarcoma, but intensive study will disclose other cellular elements with larger and poorly staining nuclei in which the ectoplasm is more extensive and irregular and shows star shaped points immediately suggesting elementary nerve cells. One will also note a finely granular substance with minute intracellular or extracellular fibrils which constitute the specific nerve fasciculus of the neuroblastoma; roset forms are common. A further fact of value is the appearance of hemorrhagic areas not only in the primary tumor but in the metastases.

Clinically the tumor presents the following characteristics:

1. It always presents during the first year or two of life.
2. It is always primary in the abdomen, usually in the suprarenals.

3. It presents an extremely malignant condition; its evolution is always rapid and in a few weeks or months produces profound cachexia.

4. Its metastases are commonly found in the liver, the flat bones and the lymph glands.

AMESSE, Denver.

INVESTIGATIONS IN PROTEIN METABOLISM IN FEVER BY THE PEPTIDASE REACTION. ISON MA, Monatschr. f. Kinderh. **36**:363, 1927.

Peptidase is a ferment bound to the body cells. Pfeiffer claims that any destruction or injury to the cells releases the ferment into the blood stream. The presence of this ferment in the blood serum should differentiate destruction of cells from nervous influences on the cells, in studies of the metabolism of fever. If the ferment is found, it would suggest that the increased protein catabolism during infection is due to actual destruction of cells.

In his studies, the author found peptidase so frequently in the blood stream and in so slight a relationship to the clinical course of the disease that he doubts whether it is really an index of destruction of cells. His study, originally intended as one of protein catabolism with reference to the peptidase index, concludes with the idea that the peptidase index is really not of great value.

GERSTLEY, Chicago.

WORK (CRYING) HYPERTHERMIA IN INFANTS. H. RIETSCHEL, G. PRINKE and F. STRIECK, Ztschr. f. Kinderh. **43**:221 (March) 1927.

The authors found it extremely easy to demonstrate the influence of body activity on the temperature of the infant, not so much in breast-fed children fed on milk poor in albumin and whey as in children who are disposed to have dyspepsia and infections. In artificially fed infants in which small rises of temperature are concerned, it is always worth while to think of the possibility that fever may be caused by crying, and that a genuine fever may likewise be intensified. It may occur with especial ease if the infant is in a stage of relative loss of water. Moreover, work fever must be considered in the calculation of food mixtures. With a twenty-four hour basal metabolism of 360 calories, work of one hour's duration means the production of 15 large calories; that is, an increase in the basal metabolism of 100 per cent. Infants who cry for long periods have an extraordinarily increased need for food; sick children who are restless have the same need. Would it not be wise to consider this factor and to make more use of sedatives in such conditions, in order to lessen the load on the intestine? One should always remember to give the infant plenty of water to provide means for giving off increased heat.

MEASUREMENT OF STRENGTH OF THE HAND AND OF VITAL CAPACITY OF THE LUNGS IN CHILDREN AND YOUNG ADULTS. EUGEN SCHLESINGER, Ztschr. f. Kinderh. **43**:232 (March) 1927.

In a survey of the status praisens of healthy school children and young adults, the determination of the strength of the hands and of the vital capacity of the lungs as functional tests represent a real summing up of accurate biologic measures. They not infrequently demonstrate an unsuspected inferiority in capacity of performance. The spirometer measures the extent of inspiratory excursions, in comparison with the circumference of the chest, especially in young girls, with much more accuracy and reliability. In spite of considerable variation in values, several conclusions may be drawn. Results are obtained for both methods which are in close agreement with one another. The values are dependent in childhood on age, on stage of development and on sex, so that boys are superior to girls in all age groups apart from the group aged 13 years. The values in relation to the size of the body are close. The children and adults who are disproportionately tall show lower values than children of the same age and length who are well proportioned. The relations

of strength of the hands and vital capacity are not so close to the body weight, since a thick padding of fat interferes a good deal with the muscular strength as well as the vital capacity. Athletic ability and regular exercises are especially marked in their influence. It is unfortunate that the spirometer is frequently contraindicated in the sick room.

HEMOGLOBIN RESISTANCE. NORA WUNDT, Ztschr. f. Kinderh. **43**:297 (March) 1927.

Fetal blood behaves like blood from the umbilical cord in regard to the resistance of hemoglobin to a solution of sodium hydrate or to acetic acid. In infants, however, blood from the bone marrow has less resistance than that of the circulating blood in the same infant. Resistance diminishes with increasing age. Beyond the first year, the disintegrating value of blood from the circulation, from the liver and from the bone marrow shows results that are in close agreement, but in pathologic cases there is an increase in resistance of blood from the liver and from the bone marrow. Since bone marrow contains not only newly formed but fetal hemoglobin as well, the disintegrating value of blood from the bone marrow cannot be the same as that of adult blood. It is astonishing that the hemoglobin resistance of blood taken from bone marrow does not diminish more quickly. One must conclude that after birth not only unstable hemoglobin is produced but blood that is resistant for a long time.

EMERSON, Boston.

METHODS OF PURIFYING SMALLPOX VACCINE. KAREL URBANEK, Čas. lék. česk. **64**:1591 (Oct.) 1925; 1635 (Nov.) 1925.

A review of the technic of vaccination is given from the arm to arm method of Jenner. A complete resumé of the methods of purification is given under physical, chemical and biologic subdivisions. A bibliography of seventy-two references is appended.

STULIK, Chicago.

OCCULT HEMORRHAGES: THE NATURE OF THE DERIVATES OF THE BLOOD PIGMENT FOUND IN THE FECES IN CASES OF OCCULT HEMORRHAGES. I. SNAPPER and S. VAN CREVELD, Nederl. Tijdschr. v. Geneesk. **71**:401, 1927.

THE CLINICAL SIGNIFICANCE OF THE OCCURRENCE OF OCCULT BLOOD IN THE FECES, Ibid. p. 525.

In an introduction to these articles the necessity of using the spectroscopic method when the feces must be examined for the presence of occult blood is emphasized; stress is laid on this point because the hemoglobin may be partly or totally broken down to the iron-free derivate, the hematoporphyrine, which does not give the oxidase tests.

In the first article the recent investigations (Schumm, Fischer and others) on the spectroscopic properties of the blood pigments found in the feces are discussed in detail, and the possible clinical significance of these researches is illustrated. Provisionally, however, the accurate analysis of the derivates of the blood pigment found in the feces has for the greater part a scientific significance, but the possibility cannot be excluded that it has also a clinical significance.

In the second article the clinical significance of the occurrence of occult blood in the feces is discussed in detail, especially the value for the diagnosis of organic lesions in the alimentary tract (ulcus ventriculi and duodeni, carcinoma intestini).

In concluding, the significance in children of the examination of the feces for occult blood is discussed. It is pointed out that in pediatrics several conditions occur which may give rise to the occurrence of small hemorrhages in the intestine.

The systematic examination of the feces might help in such cases. It is also mentioned that the beginning of the complaints of adult patients with ulcers of the duodenum not rarely dates from their childhood.

The investigation of Ratnoff is cited. He found that occult blood may be found in the feces of healthy infants and children up to the age of 6 years. The investigation of Ratnoff could be confirmed by the authors, and the nature of the derivative of the blood pigment found in the feces was further investigated in these cases. The explanation of the fact is still obscure.

S. VAN CREVELD, Amsterdam.

Nutrition

THE ANATOMY OF DIGESTION. T. WINGATE TODD, Northwest Med. **26**:507 (Oct.) 1927.

In a series of alimentary roentgenologic studies on medical students, Todd found all parts of the tract sensitive to emotional and nervous conditions. The stomach becomes atonic in outline, but not in movement or emptying time. The doudenum shows pseudostasis. The transverse colon exhibits a spasm which may inhibit onward passage of contents. The normal position of the small intestine is in the pelvis and is disposed in ladder coils. Peristalsis in the lower ileum may be slow when the transverse colon is spastic. The cecum, ascending colon and transverse colon show a peristalsis like that of the stomach and small intestine, but is slower than that of the stomach.

SCOTT, Philadelphia.

FEEDING PROBLEMS IN PRIVATE PRACTICE. ALTON GOLDBLOOM, Canad. M. A. J. **17**:1048, 1927.

The author discusses in a general way the problems of infant feeding as presented in the ordinary daily practice. He stresses the importance of individual study and the adaptation of the feeding to the individual case rather than the adherence to certain rules.

Illustrative cases are presented.

MOORE, Omaha.

THE ACTION OF ATROPINE ON MILK SECRETION. RALPH STOCKMAN, Edinburgh M. J. **34**:340 (June) 1927.

Quoting the varying opinions of authorities concerning the possible antigalactagogue action of atropine and belladonna, Professor Stockman follows with the report of the hypodermatic administration of atropine, $\frac{1}{100}$ grain (0.0006 Gm.) twice daily to fifty-two mothers during the first seven days after delivery. He feels certain that atropine arrests the secretion of milk.

NEFF, Kansas City, Mo.

I. THE STUDY OF DIGESTIVE DISTURBANCES OF THE INFANT. P. ROHMER, Rev. franç. de pediat. **3**:275, 1927.

In an introduction to this study, Professor Rohmer emphasizes the importance of differentiating between the essential characteristics of the various digestive disturbances and the incidental symptoms.

II. THE CLINICAL VALUE OF AZOTEMIA IN DIGESTIVE DISTURBANCES OF THE INFANT. P. ROHMER, Rev. franç. de pediat. **3**:277, 1927.

In a study of thirty-one cases, a definite relationship was not found to exist between the presence or the type of a digestive disturbance and the retention of urea.

III. The Clinical Value of the Phenomenon of Acidosis in Digestive Disturbances of the Infant. P. Rohmer, Rev. franç. de pediat. **3**:286, 1927.

The p_H of the blood does not show a definite relation to the nitrogen retention. Acidosis is found only in the condition designated as cholera infantum.

IV. The Definition of True Athrepsia and Its Prognosis. P. Rohmer, Rev. franç. de pediat. **3**:410, 1927.

True athrepsia should be distinguished from simple inanition, as it is a serious and prolonged disturbance of digestion and nutrition which strikes the infant during the first months of his existence. Athrepsia is, however, essentially curable with proper care and feeding, and one may conclude that the cellular functions which are essential to life remain intact.

V. Dehydration and the Choleriform Syndrome. P. Corcan et F. Klein, Rev. franç. de pediat. **3**:416, 1927.

Dehydration was produced experimentally by concentrated feedings and insufficient water. The infants showed extreme agitation, fever, loss of weight, and slowing of the capillary circulation, but they did not develop digestive disturbances or coma, and the acidosis which one finds in cholera infantum was not present. Hence it would seem fairly definite that the acidosis of cholera infantum, is not due to dehydration or slowing of the capillary circulation.

Leslie, Chicago.

I. Experimental Rickets. P. Gyorgy and S. Popovicin, Jahrb. f. Kinderh. **112**:23 (March) 1926.

Rats were fed on rickets producing diets. Control rats were divided into two groups, one receiving only the rachitic diet, while the other had additions of salad oil. The other animals received from 0.15 to 0.50 cc. of cod liver oil every second day and oil and ultraviolet ray treatments at a distance of 40 cm. for from three to five minutes also every other day.

The control rats developed rickets. Rats fed on cod liver oil did not develop rickets. Rats fed on oil irradiated once with ultraviolet rays did not develop rickets. The authors also fed rats rat skin which had been given one ultraviolet ray exposure after being cut in 30 cm. lengths. Seventy-five grams of this was fed every second day. Rats fed similarly on nonirradiated skin developed rickets. Injection of thymus extract failed to prevent rickets in rats fed on the rachitic diet.

II. Experimental Rickets. P. Gyorgy, M. Jenke and G. Popovicin, Jahrb. f. Kinderh. **112**:35 (March) 1926.

Rats on a rachitic diet were also given irradiated cholesterol and some of its derivatives, palmitic acid cholesterin ester, B. Cholesterol, pseudokoprosterin, carbonic acid and the cholesterin-free acholic fraction of gallstones. Only the irradiated cholesterol and the palmitic acid cholesterin ester prevented rickets; all the other irradiated substances mentioned caused rickets. This may be due to a change in the double binding produced by the ultraviolet rays, which is found in the cholesterol and cholesterol ester molecule but not in the other derivatives used.

Ehrmann, Chicago.

The Increase of Soluble Nitrogen in the Infant's Stomach. Rudolph Hiss, Monatschr. f. Kinderh. **36**:208, 1927.

In studies of the digestibility of cow's milk and breast milk, the author tried the experiments of removing the contents of the stomach, determining

the soluble nitrogen, allowing the mixture to stand in an incubator two hours and redetermining the nitrogen.

The subjects were chiefly infants under 3 months of age. The experiments showed the following:

Control experiments on cow's milk did not show a change in a test tube after two hours. The addition of rennin or hydrochloric acid did not cause a change. The combination of rennin and hydrochloric acid, however, caused a 50 per cent increase, which was surprisingly increased to 83 per cent when the acid was added first and then the rennin.

Control experiments in the test tube on breast milk gave identical results. There was a noticeable increase only with the combination of rennin and hydrochloric acid.

In the experiments on the contents of the stomach on cow's milk, the addition of acid caused an immediate increase of 32 per cent. Incubation did not cause a change, but the addition of acid at the end of incubation caused a further increase.

Breast milk gave identical reactions.

These experiments are confirmative of much clinical reasoning, namely, that in the infant gastric digestion is of little importance. To have a considerable increase of soluble nitrogen rennin seems necessary. As this applies also to the breast-fed infant, any considerable gastric digestion would require an aphysiologic diet.

METABOLISM INVESTIGATIONS IN ADIPOSE CHILDREN AT PUBERTY. GEZA PETENYI and HEINRICH LAX, Monatschr. f. Kinderh. **36**:381, 1927.

Metabolism in adipose children at puberty is diminished. The normal metabolic increase at puberty is absent. Hence, metabolic investigation as a means of differentiating pituitary adiposity is not useful at this age.

METABOLISM AT PUBERTY. HEINRICH LAX and GEZA PETENYI, Monatschr. f. Kinderh. **36**:385, 1927.

In a considerable number of cases, metabolism at puberty is increased. The specific dynamic reaction, namely, an increase of 40 per cent following a breakfast of 200 Gm. of meat, 200 Gm. of potato and 50 Gm. of bread, is absent. Hence this specific reaction is not of value in determining pituitary disease at puberty.

GERSTLEY, Chicago.

PHOTO-ACTIVITY — ANTIRACHITISM. E. REKLING, Acta radiol. **8**:147 (July) 1927.

Experiments on rats showed that there was no relationship between photo-activity and antirachitic properties of cod liver oil and other materials irradiated with ultraviolet rays.

FOERSTER.

Prenatal Conditions

FETAL ACHONDROPLASIA. G. BERGHINZ, Clin. Pediat. **9**:119, 1927.

The patient was first seen at the age of 14 months, and the following measurements were taken: Length of the upper extremities, 17 cm.; length of the lower extremities, 20 cm.; circumference of the thorax, 40 cm.; circumference of the head, 46 cm.

Therapy consisting of thyroid extract and phosphorus was instituted. At 8 years of age, the same patient presented the following dimensions: Height, 89 cm.; length of the upper extremities, 24 cm.; length of the lower extremities, 37 cm.; circumference of the thorax, 53 cm. The circumference of the head remained unchanged.

ZAMBARANO, Northville, Mich.

A Case of Diaphragmatic Hernia. D. P. D. Wilkie, Edinburgh M. J., Tr. Medico-Chir. Soc. Edinburgh **34**:142 (Aug.) 1927.

A boy who had been cured of right diaphragmatic hernia after two operations was presented by Professor Wilkie. The diagnosis was made at 13 years of age when the boy's abdomen was explored to find the cause of repeated attacks of vomiting since birth. At the age of 17, a return of symptoms and the presence of the stomach in a sac above the level of the right side of the diaphragm as shown by roentgen-ray examination, caused Wilkie to operate through the chest, although he made an abdominal opening also. Strips of fascia obtained from the thigh were used in bridging the gap in the diaphragm. The stomach was sutured to the abdominal wall. Recovery and results were satisfactory, and the youth had been working for three months. Wilkie concludes that operating through the chest, under intratracheal anesthesia is easier and more desirable than the abdominal route.

A Case of Oxycephaly. W. J. A. Coldstream, Edinburgh M. J. **34**:357 (June) 1927.

This is the report of the comparatively rare case of true oxycephaly with the typically shaped head, syndactylism of the hand and pseudomongolian incurving of the little fingers. The family history shows the only abnormality to have been an incurving of the little fingers in a paternal grandfather and syndactyly of the same left fingers in a paternal uncle. One other child has incurving of the little fingers. The photographs and measurements of the head are characteristic. Vision is defective, but the author regards the presence of a binasal hemianopia in this patient as a unique complication of the disturbances of the eye in oxycephaly.

Neff, Kansas City, Mo.

Injury to the Liver at Birth Giving the Clinical Picture of Congenital Absence of the Bile Ducts. K. Lackschewitz, Monatschr. f. Kinderh. **36**:358, 1927.

Lackschewitz reports a case with autopsy. Symptoms were due to an enormous hematoma in the liver.

Gerstley, Chicago.

Diseases of the New-Born

Interesting Comparisons in Feeding Schedules for Full Term New-Born Infants. Edna M. Hayward and Louise Mowbray, Boston M. & S. J. **197**:515 (Sept. 29) 1927.

Previous to Aug. 1, 1926, every infant in the Wesson Maternity Hospital was nursed every three hours at one breast for twenty minutes, and then was returned to the nursery, "where, for the first seven days following delivery, he routinely received a supplementary feeding of whey, provided no other p.c. formula was ordered by the doctor. Between feedings the usual sterile water was given."

Beginning with August 1, the infants were nursed every four hours for ten minutes at each breast, with a supplementary feeding when necessary. During the first three days after delivery, 5 per cent lactose solution was given alternately every four hours with the regular breast feeding.

The following statistics are taken from two groups of 371 unselected infants seen consecutively who were on the three and four hour feeding schedules: 90 infants were discharged after from nine to eleven days on the three hour schedule; 42 had been given supplementary formulas; the weight was the same as the weight at birth in 11, above it in 15 and below it in 64. Ninety infants were on the four hour schedule; 8 of these had been given supplementary formulas, the weight was the same as that at birth in 12, above in 40 and

below in 38. In a total of 205 infants discharged after from twelve to thirteen days on the three hour schedule, supplementary formulas had been given to 103; the weight was the same as that at birth in 17, above it in 61 and below it in 127. In a total of 205 on the four hour schedule, supplementary formulas had been given to 13; the weight was the same as that at birth in 31, above it in 99 and below it in 75. In a total of 76 infants discharged after from fourteen to fifteen days on the three hour schedule, supplementary formulas had been given to 28; the weight was the same as that at birth in 4, above it in 28 and below it in 44. In a total of 76 on the four hour schedule, supplementary formulas had been given to 8; the weight was the same as that at birth in 12, above it in 43 and below it in 21.

In regard to the three hour schedule, "two facts were outstanding: A large percentage of the babies in the nursery were being wholly or partly formula fed. (By formula other than whey.)

Too large a percentage of breast fed babies were being discharged never having regained their birth weight.

Furthermore, the greater number of feedings caused frequent handling and transferring of the babies to and from the nursery. This left only extremely short intervals when they were undisturbed and also interfered with the routine care and treatment of mothers."

In regard to the four hour schedule "the longer intervals between feedings give the babies longer consecutive periods of rest and they are handled much less. As the baby nurses both breasts at every feeding, at no time between feedings is either breast excessively full and the mother is able to enjoy greater comfort. Due to increased stimulation more mothers are now able to breast feed their infants and an exceedingly small percentage of breast fed babies is discharged under birth weight. The number of p.c. formulas has been greatly diminished."

GENGENBACH.

HEMORRHAGE INTO THE LUNGS OF NEW-BORN INFANTS. K. WALCHER, Deutsche Ztschr. f. d. ges. gerichtl. Med. **8**:523, 1926.

From a careful gross and microscopic study of the hemorrhages in the lungs of 245 maturely or prematurely born infants dying during or soon after birth, not much that is new is suggested to explain their origin. They are practically constant with premature birth and attributed to the greater ease with which the lungs may be torn by pressure in the birth passage at such periods of incomplete development and lesser ability to resist external violence. The subpleural ecchymoses are often found continued into the lung tissue as broad bands of hemorrhage in septums and about blood vessels. The blood is well absorbed at the end of the second or third week after birth, but frequently the regions of hemorrhage are infected and then more bleeding occurs. Infarcts are simulated.

Only subpleural hemorrhages were found in one of two infants suffocated after birth at term, there were no hemorrhages in the lungs of the other. With death from natural causes taking place slowly as it frequently does in infections, the lesser cardiac force causes both stasis and hemorrhage. The hemolysis accompanying putrefaction prevents recognition of hemorrhages in decomposed bodies.

THE FORENSIC IMPORTANCE OF THE MICROSCOPIC EXAMINATION OF THE LUNGS OF INFANTS DYING AT OR ABOUT THE TIME OF BIRTH. J. OLBRYCHT, Deutsche Ztschr. f. d. ges. gerichtl. Med. **9**:529, 1927.

The length of the femurs, characteristics of meconium in the bowel and microscopic examination of the lungs served to demonstrate live birth at term of a child whose body was extensively burned to conceal murder by the mother. The outside of the lungs was cooked and gray for from 2 to 7 mm., but in many deeper places the alveoli were found well distended and the bronchioles circular

in place of the stellate fetal form from infolding of the lining. Many experiments were made by burning and partly cooking fetal human and bovine lungs into which it was definitely known air had never entered by respiration; such lungs were then examined in many places microscopically. Olbrycht also refers to results of the histologic study of the lungs in the routine examination of 188 fetuses and new-born infants.

From such studies the conclusion is expressed that microscopic examination of the lungs, if properly done so that the condition in many parts of both lungs is ascertained, affords the best means of demonstrating that respiration occurred. Postmortem gas production produces cavities in the interstitial septums, and superficial respirations followed by death cause distention of only certain portions. Other tests are not altogether deprecated, but this "histologic test" is the most trustworthy. It should be used in conjunction with microscopic examination of meconium, and whatever fluid there is in the lungs, also with the time honored hydrostatic tests.

E. R. Le Count.

Blood Platelets in Newly Born and Very Young Infants. Helene V. Farnos, Jahrb. f. Kinderh. **112**:47 (March) 1926.

According to Farnos' method, the following counts of blood platelets were found in 132 cases: From 100,000 to 200,000 on the first day in the newly born; from 170,000 to 270,000 at the fifth to the seventh day; from 250,000 to 350,000 in the third week.

In icteric children, the highest count is 150,000 and reaches the normal somewhat more rapidly in the third week. The platelets rise as the red cells fall. In a case of melena neonatorum, the red cells fell as the platelets rose. In infections, the thrombocytes fall.

On the first day, the red cells had the following relationship: Normal, from 55 to 65 per cent; large, from 15 to 25 per cent; net-forms, from 18 to 25 per cent; nucleated red cells, from 4 to 6 per cent; megalocytes, from 3 to 8 per cent.

Ehrmann, Chicago.

Asymmetry in the New-Born Skull. Hans Abels, Wien. klin. Wchnschr. **40**:1217 (Sept. 29) 1927.

On the basis of a survey of the literature as well as personal observations in 6,000 new-born infants, Abels discusses factors in the production of asymmetry in the skulls of the new-born. Passage of the head through the birth canal causes only transient cranial deformities. Those which persist after the first week of life are to be considered as prenatal. They are produced in the later weeks of intra-uterine life.

Asymmetries of the skull are most frequently encountered in head presentations. The commonest form exhibits flattening of the posterior portions of the parietal bones, compensatory bulging of the frontal bones and distortion of the great fontanel. Abel believes that these changes are due to the nonsymmetric position of the uterus, which causes certain parts of the head to impinge on the maternal bony pelvis. The lower uterine segment may act as an additional factor in the production of these changes. The author was able to demonstrate that certain obstetric positions of the head were responsible for corresponding forms of asymmetry. Even breach-born infants often exhibited a characteristic cranial deformity which he considered due to pressure of one side of the face and skull against the fetal shoulder during the late months of pregnancy.

The author admits the possibility of an hereditary or constitutional factor in the production of asymmetric skulls. He has usually found such deformities to be associated with signs of deficient ossification of the cranial bones. Apparently, the mechanical factors already mentioned are able only to act on soft skulls, since new-born infants with hard, well ossified heads practically never

show asymmetry. Abel holds that the endogenous factor responsible for faulty ossification may not be an hereditary one in the narrow sense of that term, but may be related to faulty maternal diet, lack of vitamins, or insufficient ultraviolet rays.

OLMSTED, Seattle.

LOBAR PNEUMONIA IN NEW-BORN INFANTS. A. LAUCHE, Ztschr. f. Geburtsh. u. Gynäk. **91**:627 (Sept.) 1927.

Nine cases of lobar pneumonia in new-born infants which have been reported in the literature are reviewed. In all of them the mother had lobar pneumonia. The infants died before the third day. The author feels that the development of a lobar pneumonia is explicable on the basis of a partial passive immunization of the fetus by previous infection of the mother with the same strain of pneumococcus which caused the fatal pneumonia in the infant. In animals a partial immunization is necessary before an experimental pneumonia can be produced.

M. B. BRAHDY, New York.

TWO CASES OF MULTIPLE ABSCESSES IN THE NEWLY BORN. AXEL FRIEDLANDER, Acta Paediat. **6**:433, 1927.

These cases demonstrate the well known fact that infection may occur through the umbilicus and yet the umbilical vessels be found normal at autopsy. The most striking lesions in both cases were multiple focal necroses in the liver.

HOLT, Baltimore.

Acute Infections

INTRADERMAL SALT SOLUTION TEST IN SCARLET FEVER. BEATRICE R. LOVETT, Am. J. M. Sc. **173**:539, 1927.

The time required for disappearance of the wheal made by injecting 0.2 cc. of 0.8 per cent sodium chloride solution, intradermally, was found to be shortened in scarlet fever, and roughly so in proportion to the severity of the disease. In the absence of complications, the time returned to normal rapidly, usually before the patient was ready to be out of bed. Urticaria was associated with shortened time of disappearance. In the early stages of the attack marked shortening of the time for the disappearance of the wheal is an indication for giving antitoxin.

[ARCH. PATH.]

NERVOUS COMPLICATIONS OF VARIOLA, VACCINIA AND VARICELLA. R. E. WILSON and F. R. FORD, Bull. Johns Hopkins Hosp. **40**:337, 1927.

A diffuse nonsuppurative encephalomyelitis occurs as a rare but specific complication of variola, vaccinia and varicella. In cases associated with vaccinia, vaccine virus has been demonstrated in the nervous tissues. As yet anatomic studies apparently have not been made on encephalomyelitis associated with varicella (no deaths in twelve cases). It is possible that cases of encephalomyelitis in vaccinia have been mistaken for tetanus.

[ARCH. PATH.]

VARICELLA IN MONKEYS; NUCLEAR INCLUSIONS PRODUCED BY VARICELLA VIRUS IN TESTICLES OF MONKEYS. T. M. RIVERS, J. Exper. Med. **45**:961 (June) 1927.

The eosin-staining nuclear inclusions found in monkeys' testicles in these experiments are believed to be the only definite recorded proof that experimental animals are susceptible to the action of varicella virus and were found to be specifically associated with such virus.

JAMIESON, Detroit.

RHEUMATIC FEVER: BACTERIOLOGIC STUDIES OF A NONMETHEMOGLOBIN-FORMING STREPTOCOCCUS WITH SPECIAL REFERENCE TO ITS SOLUBLE TOXIN PRODUCTION. KONRAD E. BIRKHAUG, J. Infect. Dis. **40**:549, 1927.

A new species of a nonmethemoglobin-forming inulin-fermenting bile-insoluble and toxigenic, gram-positive streptococcus was regularly isolated from the tonsillar crypts and abscesses, and irregularly from blood cultures, heart vegetations, feces and urine, of persons stigmatized by rheumatic fever and its syndromes.

Culturally, toxigenically and serologically, the nonmethemoglobin-forming streptococci constitute a closely related group of micro-organisms, distinguishable biologically from the groups of *Streptococcus viridans* and *Streptococcus hemolyticus.*

In a study of the production of soluble toxins by streptococci isolated from patients with rheumatic fever, it was found that among 98 strains of *Streptococcus hemolyticus,* toxin was not demonstrated; among 247 strains of *Streptococcus viridans,* 4.7 per cent produced toxin and among 68 strains of the nonmethemoglobin-forming streptococcus, 7 per cent were found to produce a soluble toxic filtrate, slightly weaker in potency than that produced by *Streptococcus scarlatinae* and *Streptococcus erysipelatis.*

When injections were made intradermally with 0.1 cc. of a 1:10 dilution of the toxic filtrate of the nonmethemoglobin-forming streptococcus, 18 per cent of normal adults and 11 per cent of normal children without a history of rheumatic fever gave positive skin reactions measuring more than 1 cm. in diameter within twenty-four hours after the injection.

Among persons with a definite history of rheumatic fever and its syndromes, when tested intradermally with 0.1 cc. of a 1:100 dilution of the soluble toxic filtrate produced by the nonmethemoglobin-forming streptococcus, 56 per cent of adults and 76 per cent of children gave positive skin reactions, and when tested with 1:10 dilution of the toxin, 67 per cent of adults and 85 per cent of children reacted positively with lesions measuring more than 1 cm. in diameter within twenty-four hours after the injection.

Intramuscular injections of increasing doses of the toxic filtrate in laboratory animals and in human beings susceptible to the toxin produced a neutralizing antitoxin.

Injected intravenously and subcutaneously in rabbits, the nonmethemoglobin-forming streptococcus invariably produced nonsuppurative polyarthritis, subacute bacterial endocarditis, myocarditis and epicarditis, with unique tendency to mitral stenosis, extensive mural vegetations and, occasionally, myocardial degeneration, with nodular cellular arrangements of multinuclear forms, as well as polymorphonuclear and mononuclear cells.

Injection intra-articularly and intramuscularly of large doses of the soluble toxic filtrate of the nonmethemoglobin-forming streptococcus in the author, who previously had repeatedly given a strongly positive intradermal reaction with 0.1 cc. of a 1:100 dilution of the toxin, produced a typical clinical picture of acute polyarthritis of the rheumatic type, which healed without suppuration or injury to the articular surfaces.

SEXUAL DIFFERENTIATION IN SUSCEPTIBILITY TO AND MORTALITY FROM WHOOPING-COUGH IN CHILDREN UNDER FIVE YEARS. MATTHEW YOUNG and W. T. RUSSELL, Brit. J. Child. Dis. **24**:165 (July-Sept.) 1927.

As a result of their study of the statistics dealing with the incidence and mortality of whooping cough in children in England, Scotland, Ireland, America, France and Germany, the authors found that the disease apparently exhibits a predisposition to attack females more frequently and with greater severity than males. In consequence, a higher mortality is observed in females. The reasons for this sexual difference is not known.

LANGMANN, New York.

NOTES ON JUVENILE RHEUMATISM — BEING A COMPARISON OF THE REPORTS OF THE BRITISH MEDICAL ASSOCIATION AND THE MEDICAL RESEARCH COUNCIL. REGINALD MILLER, Brit. M. J. **2**:952, 1927.

This paper is a discussion of the two reports made independently, by a special committee appointed by the British Medical Association and the Medical Research Council. In each report, there was not any mention of the other, and the personnel was different in each instance. In studying these reports, the author found 6 main points of contact. On four of these, it may fairly be claimed that agreement is shown: these relate to the influence of: (1) social status; (2) heredity; (3) school environment, and (4) tonsillar disease and tonsillectomy. In the two remaining questions, those of the influence of (5) contagion and (6) damp dwellings, agreement appears to be lacking.

1. THE INFLUENCE OF SOCIAL STATUS

Rheumatic infections were found to be more common in the poorer classes than in the well-to-do though the incidence of the disease was less in the lower than in the upper strata of the poorer classes. Both reports were in agreement with this observation.

2. THE INFLUENCE OF HEREDITY

The general conclusion arrived at on this point was that "not sufficient evidence of heredity was forthcoming."

3. SCHOOL ENVIRONMENT

School environment, in a broad sense, means the circumstances of a child living at home and undergoing compulsory education at a day elementary school. The opinion of the British Medical Association committee was to the effect that in the production of rheumatism the influence of the child's home was greater than that of its school, but that, on the other hand, the attendance at school had an important influence on increasing the severity of the infection in rheumatic children, thus favoring heart disease. The general conclusions seem to throw the emphasis back again on the "home" as opposed to the "school" itself, for this evidence points to the conclusion that children taken from the rheumatic stratum of society escaped the disease if transferred to a school which they attended from healthy "home" surroundings.

4. THE INFLUENCE OF TONSILLAR DISEASE AND TONSILLECTOMY

This opinion was based on investigations detailed in part of the report in which the attempt was made to establish through propositions (1) that the closest estimate of the value of tonsillectomy in juvenile rheumatism was to be obtained, not by a "follow up" method, but by a study of active rheumatism in children on whom tonsillectomies had been performed; (2) that if this were done, it would be found that in such cases the rheumatism was of a type milder than the ordinary, the heart being conspicuously spared; (3) that the commonest manifestation of any severity in children on whom tonsillectomies had been performed was chorea, and that this tended to be uncomplicated by heart disease.

5. THE INFLUENCE OF CONTAGION

The Medical Research Council's general conclusion in regard to the influence of contagion is "on the whole, while it cannot be said that there is, in the facts collected, any conclusive evidence of contagion, many of them are consistent with this view." In contrast to this, the following appears in the British Medical Association committee's report: "All the evidence points against the importance of direct contagion, although every one has from time to time seen two cases arising synchronously or close together in a family.

Probably we should liken Rheumatism in this respect to Pneumonia or Appendicitis rather than to Tuberculosis. Direct infection from one case to another is of no practical importance."

6. THE INFLUENCE OF DAMP DWELLINGS

The world distribution of rheumatism and its seasonal incidence in England make it almost impossible to conceive that cold and damp should not be important factors, according to the report of the British Medical Association, while the Medical Research Council reports, on the other hand, "that the housing inquiry threw but little light on the problem; dampness which has generally been credited with playing a large part in the causation of Rheumatism was only slightly more frequent in the houses of the rheumatic families than in those of the others."

According to Miller, there appears to be considerable diversity of opinion between the two reports as to what exactly constitutes dampness. The author considers also that in the last report (6), the controls were not sufficiently carefully selected by the Medical Research Council, which of course militates against their opinion as to the importance of dampness as a causative or contributing factor.

BROWN, Toronto.

THE PROPHYLAXIS OF MEASLES, WITH A SUGGESTED SCHEME IN DEALING WITH EPIDEMICS. W. S. C. CEPFMAN, Proc. Roy. Soc. Med. **20**:80 (Aug.) 1927.

A report on the infectivity of measles and mortality due to it is first given in the paper. Then a few methods of prophylaxis are mentioned. They are: (1) isolating patients suspected of having the disease and contacts for from fifteen to twenty-one days; (2) compulsory notification; (3) early visit to patient's home by health visitor; (4) provision of adequate nursing and medical attendance in patient's own home; (5) injection of serum of persons who have had the disease or who are convalescent from measles. The prophylactic dose of serum has to be increased in direct ratio to the time of exposure to the disease. The author then gives a suggested scheme for dealing with epidemics of measles in detail.

WILLIAMSON, New Orleans.

A SHORT SURVEY OF THE DIPHTHERIA PREVENTION WORK IN EDINBURGH. ALEXANDER JOE, Edinburgh M. J. **34**:347 (June) 1927.

The incidence of diphtheria in Edinburgh for the five years from 1921 to 1925 had been about six cases for each 1,000 children under 15 years of age, and the death rate slightly less than one for each 1,000 children. The Public Health Department has recently tested or protected nearly 10,000 children for the years from 1924 to 1926. About 80 per cent of those giving a positive reaction to the Schick test have been given a total of 3 cc. of tuberculin A. The percentage of positive reactions in young school children was 84.2. Among nearly 5,000 children given tuberculin A the later incidence of diphtheria was 1.8 cases per thousand without any deaths from the disease. The number of such cases was nine, seven of which occurred within six months after the attempt at active immunization. Five persons with a recorded negative reaction to the Schick test developed the disease, which the writer explains as a discrepancy due to faulty reading of the Schick reaction, or as mild cases. Joe believes that with a history of a negative reaction, a mild throat exudate with positive culture would have been more convincing for diphtheria if a virulence test had been made from the culture, a Schick test repeated before the antitoxin was given or the antitoxin content of the blood determined. However, in deciding whether a mild tonsillar exudate in these cases in which the Schick reaction to the test was negative is diphtheria, one should be cautious in making a diagnosis in the presence of a positive throat culture. These few disappointments or incongruities do not disprove the value of the new methods used in active immunization for controlling the spread of the disease.

REPORT OF AN INVESTIGATION INTO AN OUTBREAK OF INFECTIOUS JAUNDICE. T. J. MACKIE and D. G. S. MCLACHLAN, Edinburgh M. J. **34**:456 (Aug.) 1927.

Since 1924, spirochetal jaundice has been reported in individual cases and epidemics in Scotland. While a considerable number of infections have occurred among miners, over half were in persons not connected with mines, and in one series half of the cases were in children or in young adults under 20 years of age. An epidemic occurred in a boys' school in England. That rats may be carriers of the disease is probable, but the occurrence of the disease in families suggests that it may also be spread by contact from person to person. In children recovery nearly always takes place.

The laboratory diagnosis is not easy. The presence of leptospira may be demonstrated in some cases by inoculating guinea-pigs with the human blood during the first four or five days of the disease, following which the animal may die of jaundice and demonstrable hemorrhages in the lungs. Spirochetes may be found in the minute examination of the blood and tissues of the animal. After the tenth day leptospiras may be seen by dark-ground illumination of the urine. The organisms found in the urine may be altered in morphology and be less virulent, due to the effect of the urinary acid or bile constituents. Inoculation with such urine may fail to produce the disease in animals, or the characteristic jaundice may not develop.

This paper reports an outbreak of seven cases of infectious jaundice in young persons only, showing a familial incidence. Five children attended the same school, and the two other persons were adults, aged 20 and 22, belonging to one of the families.

Four of the persons resided at a farm house and the other three at a cottage 1½ miles distant. All the patients had vomiting and low fever, and had developed jaundice in from three to seven days. Headache and epigastric pain were present in some cases. All the patients had mild attacks and recovered rapidly. The diagnosis depended on the clinical symptoms and in three instances on the symptoms of atypical leptospiras in the urine. Animal inoculation was negative, except that one guinea-pig died and showed hemorrhages only of the lungs and kidneys. While the first case may have been inoculated by a rat, the later cases must have come from contact with the earlier cases. Rats were not found on the premises and the water supply, while poor, was not contaminated with leptospiras. It is known that the organism can penetrate the skin, and this may have been the case in the school or household. The authors do not feel that their observations are conclusive; yet it is not improbable that some of the outbreaks and sporadic cases of mild jaundice not infrequent in children may be leptospiral in origin.

NEFF, Kansas City, Mo.

THE ETIOLOGY OF SCARLET FEVER. H. DEICHER, Jahrb. f. Kinderh. **112**:74 (March) 1926.

Scarlet fever toxin was made by growing scarlet fever streptococci on a pancreatin broth and filtering through a Berkefeld filter. The toxin was then given intracutaneously to patients (Dick test).

Deicher is convinced of the specificity of the scarlet fever streptococcus, first because of the Dick test. The reddening caused by the injections of his toxin, prepared as described, was not due to protein, as the reddening occurred only in the unboiled toxin. The toxin which caused reddening after being boiled forty-five minutes was discarded, as the reddening was probably the result of bacterial albumin. All streptococcus toxin of the hemolytic type gives this reaction, more or less. Specificity can be seen as follows:

1. In the absence of reaction in persons convalescing from scarlet fever.

2. In the neutralization of the toxin by scarlet fever serum in the test tube, as a reaction does not follow in a susceptible person following such a mixture. The same occurs when Dochez serum is used instead of convalescent serum.
3. Marked reaction in susceptible persons causing sore throat, fever and rash.

EHRMANN, Chicago.

INTRACUTANEOUS SMALLPOX VACCINATION. FRITZ IRION, Monatschr. f. Kinderh. **36**:225, 1927.

In a study of the intracutaneous method of vaccination, the author found a dilution of one sixtieth to one eightieth the most effective. He has had good results with the method and advocates it for the following reasons: 1. The lessened constitutional reaction. 2. The diminished excursions of temperature. The children can be bathed during the entire period. 3. Scars are not present. 4. As the reaction takes place under the skin, secondary infections are not present.

MENINGITIS IN MUMPS. L. SCHOENTHAL, Monatschr. f. Kinderh. **36**:306, 1927.

Schoenthal reports the case of a boy, aged 7, who during an epidemic of mumps developed meningeal symptoms. The spinal fluid was under increased pressure and showed traces of protein and increased lymphocytes. The child recovered. The author thinks that he prevented the development of meningitis in other patients with mumps showing beginning nervous symptoms, by early lumbar puncture.

PECULIARITIES OF DYSENTERY IN INFANCY. LEO BUCHHOLZ, Monatschr. f. Kinderh. **36**:351, 1927.

The prevailing opinion is that in bacillary dysentery the urine is free from sugar. The author reports three cases of unquestionable dysentery confirmed by bacteriologic examination which showed that glycosuria was present. This is explained by the hypothesis of changed function of the liver as there was always an acute enlargement of the liver and spleen. Probably the toxin acted on the kidney also.

GERSTLEY, Chicago.

DIFFERENTIAL DIAGNOSIS OF DIPHTHERIA. G. MORAWITZ, Wien. klin. Wchnschr. **40**:1206 (Sept. 22) 1927.

Morawitz discusses the conditions of the throat that produce membranes that are likely to be confused with pharyngeal diphtheria. The almost afebrile course and sweet, acetone breath in the latter are points of importance. One must not fail to consider the possibility of combinations of diphtheria with scarlatinal or with septic (necrotic) sore throat. In such mixed infection, diphtheria may be absent from the external surface of the membrane but will be found underneath it.

The author observed twelve cases of "angina agranulocytica," which was first described by Schultz in 1912. These were characterized by membranous pharyngitis, high fever, early prostration and stuper, leukopenia and rapid disappearance of polymorphonuclear leukocytes from the blood. Streptococci were recovered from the blood in one case. Death usually occurred on the fifteenth or sixteenth day. Morawitz believes this condition to be rare in children.

Diphtheria must also be differentiated from Plaut-Vincent's angina, primary and secondary syphilis of the mouth and the lesions in the buccal cavity which are sometimes seen in the early stages of acute leukemia. The membrane that forms following tonsillectomy may also cause confusion in diagnosis.

OLMSTEAD, Seattle.

SKIN REACTION IN ALLERGIC RABBITS AS AN AID IN DIAGNOSING SMALLPOX. A. CHARLOTTE RUYS, Nederl. Tijdschr. v. Geneesk. **71**:275, 1927.

Gins has recently indicated a new method to set forth the diagnosis of smallpox within twenty-four hours with the aid of a skin reaction in rabbits, made allergic with vaccine-lymph (Zeitschr. f. Hyg. u. Infectionskrankh., June, 1926). Gins could control his method in only two cases. Therefore when some cases of smallpox occurred in Holland last year, Miss Ruys tried the method also. Eight white rabbits were vaccinated by subcutaneous injection of 1 cc. of diluted vaccine-lymph. After twenty-four days the rabbits were inoculated in the same way respectively with vaccine-lymph, the material being obtained from patients with smallpox and liquid from vesicles of subjects with chickenpox. As a control, experimental inoculations with only glycerine were made. (The scarifications must be made carefully.) Five of the eight rabbits reacted allergically both on inoculation with vaccine-lymph and with material of the two patients with smallpox, but not with glycerine nor with liquid of the chickenpox vesicles. As three rabbits had not become allergic, to all animals the same amount of vaccine-lymph was injected again, and after nine days the experiment was repeated with the material of the patients with smallpox. All rabbits were then allergic for vaccine-lymph and smallpox material. After one week the experiment was controlled, and material from patients with chickenpox was also used. The vaccine and the material from patients with smallpox gave a distinct allergic reaction; the material from patients with chickenpox did the same, but to a less degree, contrary to the statements of Gins. Still the author is of the opinion that the method may be of value in diagnosing smallpox.

THE PROBLEM OF THE "PURE" SMALLPOX VACCINE IN CONNECTION WITH ENCEPHALITIS POSTVACCINALIS. H. ALDERSHOFF, Nederl. Tijdschr. v. Geneesk. **71**:1202, 1927.

In this article the author, director of the State Serological Institute at Utrecht, describes the different means of purifying the virus, used in the vaccination against smallpox, from other living organisms: (1) mechanical means (filtration, absorption, centrifugalization); (2) chemical means (glycerin, ether, chloroform, phenol, eucupinotoxinum hydrochloricum and others); and (3) endeavors to purify the vaccine by cultivation on living tissues (tissue cultures of living animals). The question of the purification of the vaccine-virus became inperative in Holland following the development of several cases of encephalitis postvaccinalis as also reported from other countries. Aldershoff points out that the etiology of this encephalitis is still obscure; he discusses the different possibilities. The fact that about two and one-half millions of children in Spain have been inoculated since 1923 with a sterile neurovaccine prepared by Dr. Gallardo after a method indicated by Levaditi, and that cases of encephalitis postvaccinalis did not occur there, was the principal reason to propose the use of this bacterial sterile vaccine in Holland. The author describes in detail the preparation of this neurovaccine, cultivated in the brains of rabbits, the original material being obtained from Dr. Gallardo himself at Madrid. Since August 22 of this year this neurovaccine has been used in Holland. At the end of his article the author gives his opinion that if cases of encephalitis postvaccinalis occur following the use of this new vaccine, obligatory vaccination as exists in Holland cannot be maintained. (As new cases of encephalitis postvaccinalis have recently occurred following the use of this neurovaccine, the government and the medical authorities are deliberating a provisional repeal of the obligatory vaccination.)

S. VAN CREVALD, Amsterdam.

THE SUPERVISION STABILITY OF THE BLOOD IN SCARLATINA. HANS RHODIN, Acta Paediat. **7,** supplement (June) 1927.

The phenomenon of sedimentation of the red cells was studied in fifty-eight cases. A "characteristic phase" of the suspension stability curve is described, which consists in a fluctuation from a pathologically high value to a somewhat lower one, recurring every few days. The course of the curve is usually high at the onset of the disease and becomes gradually lower with convalescence.

In a number of cases, observations were also made on the blood count, the hemoglobin content, the serum proteins, the coagulation tissue and the Dick reaction. A striking parallelism was found between the suspension stability curve and the serum globulin curve. The leukocyte curve showed some similarity to the stability curve, but the agreement was less striking than in the case of the serum globulin.

HOLT, Baltimore.

Chronic Infections

THE HILUM IN TUBERCULOSIS. A. G. SCHNACK, Am. J. Roentgenol. **15**:424 (May) 1926.

The healing process in the final analysis depends on the production of an avascularity of the infected region through a production of fibrous tissue and possibly deposits of lime salts. This fibrosis generally shows definite cellular infiltration, and must be an imperfect barrier against a small but definite amount of diffusing tuberculosis and tissue toxin. The author believes that, because of its comparatively large area a widely scattered fibrotic condition will, therefore, be associated with toxic symptoms comparable to those produced by a small but definitely active lesion. "Subliminal" symptoms should not be neglected in mildly active cases with few manifestations, and these may be a lack of cardiovascular tone, fatigue, irritability, insomnia, frequent colds in the chest and in general a feeling of being "below par." The healed process is one showing a discrete, well-demarcated fibrotic or calcified area without a perifocal inflammatory zone. The degree of exudation about a focus depends on acquired and natural immunity, the strain of organism and the temporary increase or decrease in hypersensitivity. Many foci show triangular areas of varying density, confined to one or more secondary lobules of the lungs, the so-called "fans." Furry densities, especially when in the parenchyma, usually signify an active lesion. With these manifestations may be associated beading, clouding and broadening of the denser portion of the hilum shadow, and these are more significant than when the hilum shows a uniform congestion with uniformly thickened radiating markings. The latter may be due to cardiac conditions, bronchitis, asthma, pertussis bronchiectasis and mediastinal tumors.

STULIK, Chicago.

JUVENILE PARESIS. ITS SALIENT CHARACTERISTICS, WITH SPECIAL REFERENCE TO INFANTILISM. HENRY A. BUNKER, JR., Am. J. Syph. **10**:553, 1926.

Since the recognition of juvenile general paralysis by Clouston, in 1887, between 275 and 300 cases have been reported in the literature. Approximately 1.5 per cent of the children with congenital syphilis develop general paralysis, as compared to 5 per cent of the adults with syphilis. The distribution of the juvenile form between the sexes is nearly even, whereas the ratio of females to males in cases among adults has been variously estimated as 1:2, or 1:4. Other differences are a longer duration in the juvenile form, with more frequent occurrence of optic atrophy, ataxia, attacks of vomiting, convulsive seizures, hemiplegia and palsy of the cranial nerve. Retarded growth is more characteristic of juvenile general paralysis than of any other form of congenital syphilis, and this retardation is nearly always manifested by underdevelopment

of the whole person rather than of particular parts. The author reports a case showing typical features. The father had acquired syphilis nine years before the patient's birth. The patient was a full term child, weighing 7 pounds (3.2 Kg.). There was no history of convulsions, but growth was retarded, and at the age of 14 he began to show mental changes. At 16, he gave up his work, complained of difficulty of vision, showed a tendency to fabrication, ataxia, defect in speech and marked irritability, which later gave place to drowsiness. On admission to the hospital he had a spinal fluid cell count of 19, increased globulin, a general paralytic gold curve, and a positive Wassermann reaction in both the blood and the spinal fluid. He showed marked spontaneity, circumstantiality and frequently lapses in speech. The intelligence quotient was 91. Both pupils were irregular and did not react to light or in accommodation. There was slight left ptosis and a left external strabismus. The tongue deviated to the left. The Romberg test showed slight swaying. The patient was underweight and below the normal height for his age, but the ratio of weight to height was nearly normal. This patient did not respond to malaria treatment except by a slight modification of the Wassermann reaction.

JENKINS, Philadelphia.

EXPERIMENTS ON THE THERAPEUTIC VALUE OF HOT BATHS WITH SPECIAL REFERENCE TO THE TREATMENT OF SYPHILIS AND SOME PHYSIOLOGIC OBSERVATIONS. J. F. SCHAMBERG and HSIEN WU TSENG, Am. J. Syph. **11**:337 (July) 1927.

The authors give a review of the therapeutic use of hot baths. They found them to have been used by the ancient physicians of many lands. The authors call attention to the work of Schamberg and Rule, who have used hydrotherapy in the treatment of experimental syphilis in rabbits.

In the treatment of their patients, the authors gave nine baths at twenty-four and forty-eight hour intervals, depending on the reaction of the patient, the patient going into the bath with an empty stomach and the water covering his body up to the neck. Pulse, temperature and respiration are recorded before and at intervals during the bath. The initial temperature of the bath, which is from 98 to 104 F., is gradually increased up to from 110 to 114. The duration of the bath is from fifteen to forty-five minutes unless some untoward symptom develops. There is a rise in body temperature in some cases as high as 106.

This method of treatment appeared to exert a beneficial influence on the secondary lesions of the skin and to reduce the strength of the blood Wassermann reaction.

It was also noted that the hot baths caused 10 per cent decrease in the blood cholesterol and a 10 per cent increase in the blood sugar.

THE TREATMENT OF NEUROSYPHILIS. J. L. MCCARTNEY, Am. J. Syph. **11**:398 (July) 1927.

The author calls attention to the fact that about 40 per cent of all patients with syphilis have at some time had neurosyphilis. He reviews the various antisyphilitic agents and their routes of administration.

In those patients who are resistant to treatment, intraspinal or intracisternal treatment is advocated. The paper is continued in a succeeding issue.

TRYPARSAMIDE IN ACUTE SYPHILITIC MENINGITIS. E. R. SMITH, Am. J. Syph. **11**:432 (July) 1927.

The author used tryparsamide in the treatment of nine patients with acute syphilitic meningitis. The relief from symptoms has been more prompt and more satisfactory than the results obtained by other means.

The author recommends that this drug be used in conjunction with other antisyphilitic remedies. Untoward symptoms have not arisen from its use.

A Case of Sulpharsphenamine Poisoning. C. D. Post, Am. J. Syph. **11**:444 (July) 1927.

The author reports a case of encephalitis due to poisoning by sulpharsphenamine.

The patient developed headache, nausea, vomiting, convulsions and coma following the second administration of the drug. The physicians attending the patient were not informed until after his death that he had received antisyphilitic treatment.

Syphilis Transmitted by Blood Transfusion. I. I. Long and L. Gensburg, Am. J. Syph. **11**:444 (July) 1927.

The authors report a case in which an anemic man developed secondary syphilitic lesions following a transfusion of blood from his son. The transfusion failed to improve the anemia, but the subsequent arsenical therapy effected a marked improvement.

McBride, Iowa City.

Comparative Value of Methods to Reduce Harmful Effects of Neoarsphenamine by Different Vehicles. I. B. Lipskeroff and Z. N. Grebin, Arch. Dermat. & Syph. **16**:442 (Oct.) 1927.

Neoarsphenamine was administered in various vehicles other than water in an attempt to find a medium in which it may be given in larger doses and at shorter intervals without toxic effect. Of all the vehicles used, dextrose proved to be the most promising.

Effect of Elevation of Body Temperature on the Course of Experimental Syphilis in the Rabbit. Chester N. Frazier, Arch. Dermat. & Syph. **16**:445 (Oct.) 1927.

Experimental syphilis in rabbits was inhibited or suppressed by body temperatures of from 106 to 110 F. induced by bathing in hot water. Body temperatures of from 103.5 to 106.7 ("within the range of those obtainable with safety in man") were without significant influence on the clinical course of the infection.

Jeans, Iowa City.

The Bactericidal Action of Light on Tubercle Bacilli. Albert Eidinou, Brit. M. J. **2**:160, 1927.

The author states that the value of ultraviolet rays in the treatment of lupus vulgaris is well established, but the mechanism of their action is still a matter of controversy, some believing that the local application of light produces direct bactericidal action in the depths of the lupus nodule. If there is no direct bactericidal effect of these rays, some general effect on the whole body or the local effects of irradiation must be responsible for the results and cures which have been obtained.

A review of the literature indicated that the tubercle bacillus can be destroyed by ultraviolet rays, but failed to demonstrate the selective region. Further investigations were carried out.

The general conclusion of these investigations was to the effect that the cure of lupus vulgaris by means of local irradiation must be chiefly due to tissue reaction. The histologic changes following the irradiation of lupus lesions indicate an inflammatory reaction in the early stages and, later, necrosis of the chronic granulations with the formation of new connective tissue. Many theories have been advanced to explain the results which have been obtained, but definite experimental proof has not yet been described which can explain the reaction of the tissues following the general irradiation of the skin of the body, or the local application of the rays to the site of a tuberculous lesion. While the chronic tuberculous diseases of the skin and mucous membranes

respond admirably to ultraviolet radiation, the tubercle bacillus is an organism which is more resistant to the rays of the mercury vapor lamp than the staphylococcus, and apparently is only sensitive to the shorter ultraviolet rays, and from these in vivo it is protected by the tissues.

BROWN, Toronto.

A CASE OF OSTEOMYELITIS OF THE LONG BONES IN AN INFANT. THE SUBJECT OF INHERITED SYPHILIS. JAMES THOMPSON, Edinburgh M. J. **34**:466 (Aug.) 1927.

Three children in a syphilitic family had similar enlargements of the joints and bones. One of the cases is reported, showing absorption of portions of the tibial and fibular shafts, and new formation of subperiosteal bone. Rarefaction and deposition of new bone along the diaphysis of the humerus was also noticeable. Gray powder caused rapid disappearance of the swelling. The author emphasizes the usefulness of grouping all the bone lesions in congenital syphilis under the name of osteomyelitis, rather than individually as epiphysitis, osteochondritis, periostitis and osteitis, as has been the custom.

NEFF, Kansas City, Mo.

TUBERCULOUS CHANCRE IN A NURSING INFANT. MILIAN and L. DELARUE, Bull. Soc. franç. de dermat. et syph. **34**:398, 1927.

There was a brownish scaling patch the size of a pea on one ear, and the preauricular lymph node was enlarged. Animal inoculation verified the diagnosis. The mode of infection was not determined. The subject is briefly reviewed.

[ARCH. DERMAT. & SYPH.]

THE ROADS OF PROPAGATION OF TUBERCULOSIS. B. LANGE, Beitr. z. klin. d. Tuberk. **65**:278, 1926.

Severe infections of man by tactile contact or by the injection of infected food may occur only if a large number of tubercle bacilli are introduced through the mucous membranes of the upper respiratory or digestive tract. Bacilli that invade the body through such mucous membranes are apparently weakened in their pathogenicity, since they usually lead to distinctly benign forms of disease. The infection by inhalation either of dry dust or of bacilliferous droplets is of a much greater practical importance. The author believes that dust infection is much more frequent than droplet infection, since the opportunity for the former is much more readily given.

MAX PINNER.

THE ROADS OF PROPAGATION OF TUBERCULOSIS IN THE BODY. H. BEITZKE, Beitr. z. klin. d. Tuberk. **65**:291, 1926.

Since it has been definitely established that the primary complex is most frequently found in the lung, it is necessary to analyze how bacilli may reach this location. Theoretically, four avenues are possible:

1. A primary deposit either in the upper or lower digestive tract may reach the lung through the lymphatics, thoracic duct, venous blood and right side of the heart.
2. It has been claimed that they may travel from the cervical glands directly to the bronchial glands.
3. It is believed possible that they may be transported from the cervical glands directly to the apical pleura, and from there into the parenchyma.
4. Direct inhalation.

It is, however, certain that lymph vessels do not lead from the cervical glands to the bronchial glands. It is not possible to inject the tracheobronchial glands from the cervical or supraclavicular glands, not even if the

lymphatic trunk, before its opening into the vein, is clamped, since valves prevent the retrograde lymphatic stream. In cases in which both cervical and tracheobronchial glands are diseased, it is always observed that the glands decrease in size from the mandibular angle to the venous angle, and increase from here to the tracheobronchial glands, indicating two independent foci of disease. As far as the transpleural way is concerned, it must be remembered that the cervical glands have no connection with the supraclavicular glands, which alone could be held responsible for the pleural infection. In this mechanism, too, the retrograde lymph stream would have to be assumed. If one wishes to assume that the infection of the bronchial glands occurs from the mesenteric or cervical glands, one would have to prove that either of these glands are always diseased in cases of tuberculous foci in the tracheobronchial glands, since tubercle bacilli always leave their mark on the lymph glands first invaded. The fact that cases in which tubercle bacilli are found in different groups of lymph glands, in a more or less latent condition, are rare is another argument against this mode of propagation. If tubercle bacilli have first to pass lymphatic organs, their virulence is markedly decreased, particularly if they are small in numbers. The lung, however, which is not an organ of resorption, will respond much more readily to a low grade infection than the lymphatic tissue. In short, epidemiologic, experimental and anatomic studies argue strongly in favor of the primary pulmonary infection whenever pulmonary or tracheobronchial lesions are detected.

MAX PINNER.

TREATMENT OF SYPHILIS IN INFANCY. E. PESE, Jahrb. f. Kinderh. **112**:62, 1927.

Pese has treated 260 artificially fed children who had florid syphilis; 190, or 72.2 per cent, have died.

Up to 1916 (the prearsphenamine period), 65 children were treated, 46, or 70.8 per cent, of which died. After 1916, 156 children were treated; 95, or 60 per cent, died.

Pese saw 45 children repeatedly from the ages of 1½ to 13 years. He draws his material from those adequately treated, some with mercury alone, others with mercury and small doses of arsphenamine and others with large doses of arsphenamine after the manner of Erich Miller. Twenty children, or 44.4 per cent, were mentally defective. Five children received only mercury; one of these was mentally defective, and one, an unusually brilliant student. All of these have negative Wassermann reactions except the mentally defective child. Eight children had spinal tests, all of which were negative, even in a child with a saddle nose; two of these received mercury rubs only. Arsphenamine has decreased the mortality from 70 to 60 per cent, but idiocy has increased. Pese considers the prognosis as to life just as good with mercury as with mercury combined with arsphenamine and better as to mental progress when mercury alone is used.

EHRMAN, Chicago.

CONGENITAL TUBERCULOSIS. K. SCHEER, Monatschr. f. Kinderh. **36**:285, 1927.

In a clinicopathologic study, the author records four cases of congenital tuberculosis. This raises the number of authentic reports from thirty-eight to forty-two. One autopsy showed the usual changes of periportal tuberculosis. In the others, however, the primary focus was in the respiratory tract. This investigation lessens the value of exclusive examination of the portal region for congenital tuberculosis. One must now recognize two main forms: (*a*) Placental infection with pathologic changes in the liver; (*b*) primary location in the respiratory tract due either to placental infection or inspiration of amniotic fluid.

These congenital cases form 5 per cent of the total cases in infants under 1 year from 1915 to 1926. Congenital tuberculosis, therefore, is not as rare as has been previously thought.

Clinically, the disease is practically impossible to diagnose. Children are usually premature and develop normally for the first few weeks.

GERSTLEY, Chicago.

THE PIRQUET IMMUNOBIOLOGIC DIAGNOSIS OF TUBERCULOSIS IN INFANCY. F. SKALNIK, Čas. lék. česk. **64**:1375 and 1408 (Sept.) 1925.

The author regards the Pirquet test as sensitive in infancy, but he believes that intracutaneous or subcutaneous tests should be relied on in adults. Diagnostic methods should show (1) primary tuberculosis, (2) whether the present illness is due to tuberculosis or (3) whether a focus is increasing or healing. The anteallergic period depends on the infective dose, on the resistance of the body, the virulence of the organism and on the port of entry. Experimentally, the author finds that this is about twenty-nine days, though other observers have established periods as short as ten days and as long as eleven months. The antemortem period during which negative Pirquet reactions occur is also variable, so that both anteallergy and anergy must be considered in diagnosis. As a prognostic sign we must differentiate between a negative anergy due to tuberculosis or one due to some other disease. A decreased reaction to 2 mm. is cited in a child, aged 15 months, convalescing from measles, diphtheria and serum sickness in the presence of a temporary aggravation of the primary focus. Of eighty-five children under 18 months of age thirty-five had only the positive reaction to the Pirquet test and fifty had clinical tuberculosis. Sixteen of these fifty were under 6 months of age and thirty-four were over 6 months; twenty-four were well nourished and twenty-six were poorly nourished. In an infant less than 56 per cent underweight negative anergy can be ruled out in the presence of a negative reaction to the Pirquet test. Aside from cachexia, tissue turgor, toughness, pigmentation and moistness of the skin, fulness of the skin capillaries and the vasomotor condition must be considered. The actual material used is also a factor as shown by a positive and a negative reaction in the same patient when two preparations were used, simultaneously. A positive Pirquet reaction in infancy means a tuberculous infection, while a negative test is of value only after ruling out anteallergy, negative anergy and the reaction of the material. Case reports are presented, and a bibliography of seventy-five references is included.

STULIK, Chicago.

Internal Diseases

A STUDY OF THE HUMAN PLEURA PULMONALIS: ITS RELATION TO THE BLEBS AND BULLAE OF EMPHYSEMA. WILLIAM SNOW MILLER, Am. J. Roentgenol. **15**:399 (May) 1926.

The author describes a wrinkling of the pleura, freely movable over the underlying pulmonary substance, more or less circular in outline and varying from 1 to 5 centimeters in diameter. These "blebs" were associated with an emphysema and are probably an interstitial emphysema, produced by rupture of an alveolus into the areolar layer of the pleura. The question of these "blebs" producing "annular shadows" and simulating "small pneumothoraces" is raised.

LUNG ABSCESS FROM THE MEDICAL STANDPOINT. RICHARD A. KERN, Am. J. Roentgenol. **15**:407 (May) 1926.

Abscess of the lung may follow infectious conditions such as those resulting from pnuemonia, tonsillectomy or inhalation of a foreign body. The diagnosis may be difficult without roentgen-ray study because of the multiplicity of symptoms, which are somewhat dependent on the etiology. From the standpoint of prognosis, an abscess of the upper lobe is more likely to have adequate

drainage; one close to the hilum of the lung is close to the large bronchi and not only is likely to drain spontaneously but is in excellent position for bronchoscopic approach, while an abscess close to the periphery is in connection with small bronchi and can rarely be readily emptied or reached with the bronchoscope. The latter abscesses usually require surgical intervention. Medical treatment includes (1) postural drainage, (2) rest, (3) diet, (4) autogenous vaccines, (5) iron, arsenic and bitter tonics and (6) bronchoscopic treatment. Chevalier Jackson says that cough sedatives given in excess lessen natural drainage, but should be used judiciously to insure sleep.

THE ROENTGEN-RAY DIAGNOSIS OF LUNG ABSCESS. HENRY K. PANCOAST, Am. J. Roentgenol. **15**:411 (May) 1926.

Roentgen-ray study of abscess of the lung should follow a careful clinical study. The causes of pulmonary abscess are (1) pneumonia, (2) blood stream infection, (3) inspiration of septic material, (4) foreign bodies, (5) respiratory infections other than pneumonia, (6) lymphatic extension from adjacent carcinoma and (7) direct perforation from carcinoma of esophagus. Differentiation of acute consolidation may have to be made on the basis of the clinical aspect or at times bronchoscopy to differentiate abscess and tumor. Formation of cavities is readily shown in old cases, but examination may have to be repeated almost daily in early cases. The peripheral congestion may simulate consolidation and give the impression of more extension than is actually present. Termination as shown by the roentgen ray may be (1) rupture into a bronchus, (2) resolution or drainage under bronchoscopy or operation, (3) spontaneous recovery, (4) rupture into pleural cavity and (5) multiple formation of abscesses and chronic interstitial pulmonitis, possibly followed by bronchiectasis. Roentgen-ray examination is important for (1) diagnosis of the condition, (2) location and extent of the abscess and (3) study of the progress under treatment.

STULIK, Chicago.

TRANSFORMATION OF A MALIGNANT PARAVERTEBRAL SYMPATHICOBLASTOMA INTO A BENIGN GANGLIONEUROMA. HARVEY CUSHING and S. BURT WOLBACH, Am. J. Path. **3**:203, 1927.

A paravertebral swelling at the sixth thoracic level occurred in the back of a child, aged 2 years, following trauma. The lesion proved on exploration to be a cellular sympathicoblastoma (sympathetic neuroblastoma) which was mistaken for a time for sarcoma. The tumor had apparently taken its origin from the region of an intevertebral foramen, and had extended into the spinal canal and into the spinal muscles. Apparently, under the influence of Coley's toxin, the activity of the growth subsided. Ten years later, owing to the persistence of a paraplegia, an exploratory laminectomy was performed. This disclosed the relic of the former growth, the cells of which had become completely differentiated into ganglion, capsules and neurilemma cells. Because of the unusual circumstance which permitted a study of the lesion at two remote periods, the case illustrates particularly well what has been pointed out by others—that a sympathetic neuroblastoma may be the precursor of a ganglioneuroma.

AUTHORS' SUMMARY.

RHEUMATIC HEART DISEASE. G. F. STRONG, Northwest Med. **26**:444 (Sept.) 1927.

Rheumatic infection is the commonest cause of organic heart disease. The younger the patient the more likely is the patient to be rheumatic. Other causes are mostly operative in later life. The initial rheumatic infection occurs as acute rheumatic fever, chorea, tonsillitis, myositis, growing pains, erythema multiforme or subcutaneous fibrous nodules; it is possible that cardiac disease may be the primary manifestation. A high incidence of cases occurs in homes

in which another case is present, possibly indicating that the disease is of a communicable nature. Recent evidence points to the streptococcus as a causative agent. Strong believes that damage occurs by way of the coronary circulation. The mitral valve is most commonly affected, possibly because it is the last valve to lose its fetal vasculature. The valvulitis is probably caused by emboli carried in this manner. Later submiliary nodules occur in the myocardium, and exudative and adhesive pericarditis take place. The patient who has had one or more attacks of rheumatic fever is a potential cardiac patient and should be guarded in his aftercare from exposure and overstrain. Tonsillectomy removes only one of a number of possible foci, but may be of certain benefit. Environmental factors are important, dampness and exposure especially. The most important item is prognosis. By estimation of the future functional capacity, one can plan for the patient a regimen and vocation compatible with life and comfort.

DEHYDRATION FEVER. LYLE A. GREENWOOD, Northwest Med. **26**:513 (Oct.) 1927.

Dehydration as seen in infants has not been described as a cause of fever in adults. It usually occurs as a complication in comatose and stuporous states, and the symptoms produced by it are often attributed to a terminal pneumonia. The forcing of fluids is all the more important, therefore, in states in which these are poorly taken, and hypodermoclysis may be necessary to secure their introduction. Greenwood's first patient was a man, aged 62, in whom apoplexy occurred. After three days of coma, the temperature rose to 105, and the patient appeared pneumonic. Persistent hypodermoclysis brought the temperature to normal and kept it there. When it was discontinued, the temperature returned but was reduced by further hypodermoclysis. This was continued until the patient was conscious. He made an ultimate recovery. The second case was similar. The third patient had a confirmed case of pneumonia and was in stupor. Hypodermic injection of saline solution reduced the temperature until voluntary consumption of fluid was possible.

SCOTT, Philadelphia.

THE TREATMENT OF WHOOPING COUGH. R. R. STRUTHERS, MARY CHILDS and W. R. KENNEDY, Canad. M. A. J. **17**:1042, 1927.

This paper is a summary of the authors' experience in treating patients with whooping cough. Charts are presented showing the treatment of these patients by the use of drugs, administration of ether, vaccine and roentgen-ray therapy.

The combination of large doses of freshly prepared vaccine and exposure to roentgen rays gave the most beneficial results.

The authors believe that prophylaxis is the best method of treatment. They urge strict quarantine for a period of four weeks.

MOORE, Omaha.

INSULIN TREATMENT OF DIABETES MELLITUS IN CHILDREN. KISTEN UTHEIM TOVERUD, Brit. J. Child. Dis. **24**:185 (July-Sept.) 1927.

Fifteen deaths occurred among children under 15 years of age from diabetes mellitus in Norway in 1900 and thirty-nine in 1919, an average of twenty-six for the twenty year period. A similar increase was noted in other countries and cannot be entirely accounted for by more accurate diagnosis. This study represents the results of four years' treatment with insulin of forty-seven diabetic children, twenty-four boys and twenty-three girls, aged from 1½ to 14 years, who were admitted to the pediatric clinic of the State Hospital of Norway. Heredity seemed to play a minor rôle, and acute infection within six weeks of the onset was observed in only twelve cases.

The author emphasizes one factor which may somewhat obscure the symptoms in early life and make the diagnosis uncertain for a time, i. e., the small store of glycogen in children, which will tend to keep the blood sugar at a normal level for some time. If the child has taken little food for

a few days before the urine analysis, the urine may be sugar-free and the fasting blood sugar normal even if the child has a true diabetes mellitus. The value of a dextrose tolerance test is therefore of particular importance in children.

Treatment.—If the child is admitted to the hospital during a quiescent period of the disease, the tolerance for carbohydrate is first determined, then the protein need is fixed (2 Gm. of protein per kilogram for a child over 7 years and 3 Gm. for a child under 7 years). The fat-carbohydrate relation should usually not exceed 1.75 : 1, in many instances, 1.5 : 1.

A diet on which the child remains sugar-free without the administration of insulin usually is calorically insufficient; therefore, insulin was used for every patient in the series. The caloric requirements varied from 36 calories per kilogram to 90 calories per kilogram. The average was from 50 to 60 calories. Two brands of insulin were used. Three doses one-half hour before meals were found preferable to two. It was considered of great importance to keep the blood sugar at a normal rate most of the day. Hyperglycemia was found after the protein intake in all diabetic children was tested, and a second reason for the three doses was that the low store of glycogen in childhood gives rise to insulin shock more easily with one or two large doses during the day than with three smaller doses.

Twelve children were admitted in coma. Large doses of insulin were given every three or four hours and the dosage was controlled by frequent determinations of blood sugar. Carbohydrate was given in easily digestible form, such as milk, barley soup and orange juice. Alkalis were not given during coma. The results were good with one exception, a child admitted for the second time, in coma that had lasted for four days, without having received any treatment. The child was admitted in a moribund condition and died four hours later.

Development of the Child.—Weight: On admission the child was usually in a poor state of nutrition. A rapid rise in the weight curve resulted when insulin was given. A rise in the weight curve was accompanied by a fall in the blood protein, water retention taking place during the administration of insulin. If the diet was strictly controlled and insulin given regularly, the children showed an equal and constant increase in weight corresponding to that of normal children.

Growth: The figures indicating growth fall within the normal range.

Mental Development: The mental development was normal if the child was kept on a strict diet and insulin given regularly. If the diet is not maintained, when the fasting blood sugar is above normal and sugar is excreted in the urine, the children become irritable, do not want to play and are difficult to manage.

FUNCTIONAL CARDIAC DISORDERS: SYMPTOMS, SIGNS AND TREATMENT. EDITH BRONSON, Brit. J. Child. Dis. **24**:214 (July-Sept.) 1927.

The author cautions against dismissing lightly the child with so-called "functional" cardiac disease. Many of these children complain of tiring easily, breathlessness on climbing stairs, perspiring easily, cold clammy hands and feet, dizzy spells and palpitating heart. Frequently this simply means that the child is below par and that the heart shares in this general disability. The physician should not only reassure the parent in respect to serious organic disease, but he should search for the cause of the disability.

LANGMANN, New York.

SOME OBSERVATIONS ON THE BONE CHANGES IN RENAL RICKETS. E. P. BROCKMAN, Brit. J. Surg. **14**:634, 1927.

Three cases of renal rickets in children are reported, in one of which, a case of polycystic kidney, necropsy was made. In this condition, as compared with ordinary rickets, the shaft of the bone remains straight, the deformity

being due to dislocation of the epiphysis; the marrow is replaced by fat; there is marked bone absorption with little bone formation; the arteries of the medulla are thickened, and the increase in the amount of fibrous tissue and in the number of capillaries is more extensive than in ordinary rickets. It is suggested that the changes in the bone result from a toxic condition, due to renal failure, affecting the delicate cells of the growth disk and the medulla.

BENSON BLOOM.

A CASE OF ALBERS-SCHÖNBERG'S DISEASE. H. R. SEAR, Brit. J. Surg. **14**:657, 1927.

The features of Albers-Schönberg's disease are extreme density of all the bones, especially the ends of the diaphyses; marked anemia; enlargement of the liver and spleen; pressure on the cranial nerves; hydrocephalus; interference with dentition, and necrosis of the jaw. A case is reported in a boy, aged 6 years. Necropsy was not performed.

BENSON BLOOM.

PYLORIC OBSTRUCTION IN AN INFANT FROM PRESSURE OF A DISTENDED GALLBLADDER. H. H. GREENWOOD, Brit. J. Surg. **14**:663, 1927.

The cystic duct was represented by an impermeable fibrous cord. The gallbladder was enormously distended with clear watery fluid; the antrum, pressing on the second portion of the duodenum, produced the obstruction.

BENSON BLOOM.

"GASTRIC ATTACKS" IN CHILDHOOD. DONALD PATTERSON, Brit. M. J. **1**:869, 1927.

The usual age for so-called "gastric attacks" is between 2 and 7 years. The common causes of these attacks are (*a*) infections in the respiratory or alimentary attacks, (*b*) dietetic errors and (*c*) overexertion and excitement. There appears to be no doubt in the author's opinion that the first of these causes is by far the most common.

The usual history is that a child, aged 3 or 4, who refuses its supper, seems fretful, out of sorts, feverish and alarms the household by vomiting during the evening some of the food taken at dinner. Examination usually reveals a slight elevation in temperature, dirty tongue, drowsiness, irritability and refusal of food. This picture may vary considerably depending on the underlying cause and on the particular child. Thus the child may show a slight disturbance and be nauseated only, and again the vomiting may be profuse and the bowels constipated with pale motions, or there may even be profuse diarrhea.

Tonsillitis and catarrhal conditions of the respiratory tract according to Patterson are the most frequent causes of these upsets, especially is this most likely to be the cause in thin nervous and dyspeptic children. The gastric symptoms merely mask the true nature of the disease. Recurring attacks of unrecognized pyelitis in girls are not unfrequently an incriminating factor.

Careful physical examinations should be made before the physician says definitely that the disturbance is purely of a digestive nature.

During the influenza season gastric attacks are common and receive the name of "Gastric Flu." In such cases the onset is extremely sudden, the vomiting is often accompanied by diarrhea, and there is little doubt that the mucous membrane of the alimentary tract is the direct site of the infection.

At this age period slight variations in diet will not produce gross symptoms in the average child; therefore one should not begin an examination of such a patient with the thought that he has probably overeaten. The typical patient of this type is usually a nervous boy, most often an only child, who has recurrent attacks at more or less regular intervals throughout the year, becoming less and less frequent as he approaches the school age. Consideration of this diet reveals the fact that he is overfed on milk, cream and eggs, and the overanxious

mother, seeing his frail little body, plies him with what she considers the most nourishing food. The author therefore considers fat the most offending element in this group.

In overexertion and excitement the child becomes overtired, the available supply of sugar is deficient for fat metabolism and the general body nutrition. An attack of vomiting or nausea occurs, similar to those attacks of hypoglycemia in the diabetic subject who has been given an overdose of insulin.

The therapy briefly consists in preventing the child from contact infection when possible, and in securing a healthy condition of the nasopharynx. In the second group it consists of reducing the fat and egg content of the diet and increasing the carbohydrates, especially the easily assimilable sugars and, in the last group, avoiding overexertion and excitement.

BROWN, Toronto.

ASTHMA IN INFANTS. V. ZERBINO, Nourrisson **15**:193 (July) 1927.

Zerbino takes issue with those who argue that asthma is always secondary to various forms of pathologic change in the lung. In his studies on infants, he can often exclude such infections as tuberculosis, syphilis, repeated attacks of bronchitis, pneumonia, influenza, pertussis and measles. He believes rather that in the asthmatic patient there is a dysfunction of the liver which results in toxic substances being liberated into the blood and thus reaching the lungs. The lungs in turn attempt to neutralize these foreign substances by reactions of the reticular tissues around the blood vessels and bronchi. In assuming this vicarious function, the respiratory function of the lungs is interfered with, and this is manifested clinically by an attack of asthma. In support of this hypothesis, the author calls attention to the frequent association in adults of diseases of the liver, acute or chronic, and asthma.

McCLELLAND, Cleveland.

GAUCHER'S DISEASE IN THE INFANT. C. OBERLING and P. WORINGER, Rev. franç. de pediat., 1927, vol. 3.

Four cases of Gaucher's disease occurring in infants of the same family are reported. In addition to marked enlargement of the spleen and liver, all showed a nervous syndrome characterized by a diminution of psychic functions and a muscular and reflex hypertonicity. The disease progresses in several months to a complete idiocy, a decerebrate rigidity and extreme cachexia. Death takes place before the age of 1 year. The anemia, the hemorrhages and the abnormal pigmentation of the skin are almost entirely absent in the infant. At autopsy, the gross and histologic pictures do not differ in any essential from that found in the adult. The only difference is the absence of secondary lesions and the massive character of the infiltrations with Gaucher cells in the infant pointing to a more rapid evolution of the disease. The cortical atrophy on which the nervous symptoms depend is thought to be secondary to an underlying metabolic disturbance, which is more intense in the infant.

LESLIE, Chicago.

KIRCHHEIMER FAMILIES OF BLEEDERS. W. J. KLUG, Deutsche Ztschr. f. Chir. **199**:145, 1926.

Of fifty-two families descended from the Mampel bleeder family, hemophilia is found in only twelve. Klug makes some corrections in Lossen's figures. He finds only one true bleeder marriage (marriage between bleeder and transmitter). In the hundred years during which this family has been known in the medical literature, the disease has never appeared in females or been transmitted by males or from grandmother directly to grandson. In regard to transmission by males, Klug remarks that most of the bleeders have died too young to have progeny. His statistics show, in the males, twenty-seven bleeders and thirty-nine nonbleeders; in the fifty-eight females, fourteen trans-

mitters and ten nontransmitters; the rest of the female members of the bleeder branches of this family either died young or are childless up to the present time. The presence of nontransmitting females in this family goes far to prove the validity of Bauer's application of Mendel's law to hemophilia.

[ARCH. PATH.]

ULCER OF THE DUODENUM WITH FAULTY DEVELOPMENT OF THE PANCREAS IN AN INFANT SEVEN WEEKS OLD. HANS WURM, Ztschr. f. Kinderh. **43**:286 (March) 1927.

According to Schmidt, duodenal ulcers occurred with a frequency of 1.8 per cent in 1,109 autopsies in children in the first year of life, but they probably occur more frequently. The case reported was that of an infant boy who was breast-fed and who showed a sudden loss of weight at the age of 5 weeks. He was admitted to the hospital on the fourteenth day of his illness with a temperature of 100.4, poor turgor and an ashy gray color; on the seventeenth day, he went into collapse. The clinical diagnosis was alimentary intoxication. His abdomen became distended, and death occurred six hours later. At autopsy purulent fluid was found in the abdomen and a perforated ulcer, about the size of a lentil seed, was seen on the first portion of the duodenum. Besides the perforated ulcer, ring-shaped or half circular stripes were seen macroscopically all over the duodenum; they were conspicuous because they were discolored with bile. Microscopically in these areas were shallow or deep ulcers which could not be attributed to any bacterial action. Since a disturbance in the circulation could not be demonstrated and the form of injury did not correspond to the territory of any single vessel, there remains only the assumption of an especial vulnerability of the epithelium of the duodenum. This assumption was supported by the finding of fine cystic degeneration of the pancreas with faulty development of the head of the pancreas, as there is close relation between the embryologic development of the duodenum and of the pancreas.

TWO CASES OF DYSTROPHIA ADIPOSOGENITALIS OF HYPOPHYSIAL CEREBRAL ORIGIN. ALEXANDER KROWITZKY, Ztschr. f. Kinderh. **43**:315 (March) 1927.

The disease picture of dystrophia adiposogenitalis was presented in a boy with obesity, characterized by excessive amount and by localization, ruddiness of the face and acrocyanosis, dysplastic form of the skull, hypoplasia of the genitals and hyperthermia. His sister was likewise obese but to a greater degree and showed a caput quadratum, considerable acrocyanosis, an inclination to sweat, mental retardation and epileptic spells. Roentgen-ray examination in both cases disclosed a small sella, and in both cases the sclerae were blue. These children began to get fat at the age of 6 months.

In 1901, Frölich considered that this sort of syndrome was a pure hypopituitarism, but Biedl later noted that it was not for, by a series of roentgen-ray observations, it was confirmed that the hypophysis frequently remains unchanged. When this is so, in addition to the symptoms of dystrophia adiposogenitalis, a number of degenerative and dysplastic appearances are present: atresia ani, polydactylia, retinitis pigmentosa, malformations of the skull and mental retardation. This type was regarded by Biedl and Bordet as a pure cerebral form. In the origin of the disease, a disturbance of the hormone correlation is paramount and exists between the hypophysis and the regio hypothalamica; that is, the part of the brain in which the higher vegetative trophic centers are localized for the regulation of fat, protein, salts and other constituents of the body. The whole group of symptoms which is called forth by the ineffectiveness of the midbrain as a result of its failure to develop, according to Biedl, Dr. Ratner proposes to name dysencephalic insufficiency. Zondick calls this syndrome the hypophysial-cerebral-peripheral-obesity which is based on a disturbance of the water-salt metabolism in the system, midbrain-hypophysis-periphery.

The second case may be considered an example of the cerebral form of dystrophia adiposogenitalis, since all the characteristic symptoms are sharply marked. In the first case, symptoms of hypophysial insufficiency predominate, but in consideration of the localization of fat, which is not typical for hypopituitarism, and of the color of the skin and of the familial factor, it must be admitted that insufficiency of the midbrain is also concerned. Doubtless the other glands of the endocrine system were disturbed in addition.

EMERSON, BOSTON.

UNUSUAL COMPLICATIONS AFTER INJURIES TO THE ESOPHAGUS BY FOREIGN BODIES AND IN OTHER WAYS; COMMENTS ON ROENTGEN-RAY DIAGNOSIS. WERNER KINDLER, Ztschr. f. Hals-, Nasen- u. Ohrenh. **19**:3 (May 16) 1927.

The author reports two cases: 1. A purely traumatic aneurysm of the aorta following the esophagoscopic removal of a sharp chicken-bone which had lodged at a depth of 33 cm. Nine days later, death occurred suddenly. Necropsy showed that the bone had penetrated the esophagus and injured the wall of the aorta before it was removed. Repeated clinical and roentgenologic examinations had not divulged the small traumatic aneurysm in the descending arc.

2. Diffuse mediastinitis with chronic pneumonia (carnification) after injury to the esophagus following progress of the stenosis into the area of the chest with spontaneous healing. The stenosis was caused by lye in a child, aged 3½ years, and was diagnosed by roentgen-ray examination with a contrasting substance. Treatment consisted of placing the patient in an oblique position with the head downward in order to prevent a mechanical extension of the mediastinitis, irrigation of the esophagus with a solution of permanganate of potassium and rest of the esophagus. Nourishment was provided by means of nutritive enemas. Following treatment, the stenosis could no longer be demonstrated. Five months later, at home, the child suffered from measles, complicated by purulent pleuritis. The patient died. Necropsy was not performed. Incidentally, the author states that roentgen-ray examination with the aid of bismuth was successful in an obscure case in which a simple examination with the roentgen ray and three examinations with the esophagoscope failed to establish a diagnosis. A fluoroscopic examination with bismuth showed a fine covering on the posterior wall of the esophagus at the height of the seventh thoracic vertebra. This was also found by roentgen-ray examination. The localization made it possible to palpate and remove by esophagoscopy a thin plate of bone, 2 cm. long and 1.5 cm. wide. It was buried deep in the loosened mucous membrane of the esophagus. The author speaks of the value of contrast mass in stenosis and diverticula, especially when a perforative injury of the esophagus is present or suspected. This method is especially important in severe esophagitis and peri-esophagitis with destruction of tissue, when esophagoscopy is directly injurious. In mediastinitis, a fluoroscopic examination with a contrasting substance and the patient in an oblique position gives information concerning the extent of mediastinitis. Mediastinitis, especially an infiltration of the lung, with subsequent gangrene of the same, can be recognized by simple irradiation before clinical symptoms appear.

1. Simple examination by the roentgen rays is frequently less reliable than esophagoscopy in locating foreign bodies in the esophagus, but is serviceable with the aid of a contrasting substance (Holzknecht) in diseased conditions and injuries of the esophagus, also in those caused by foreign bodies, and for an early recognition of perforations and their sequelae.

2. This procedure surpasses the autoscopic and physical examination when complications emanating from the esophagus into the mediastinum and into the lung are suspected or present.

3. The roentgen-ray method of examination can be repeated as often as desired, even in grave diseases, for observation of the further course of the disease, because it does not cause any pain and is not fraught with danger.

AMBERG, Detroit.

A CASE OF PURPURA FULMINANS WITH SYMMETRIC BLEEDINGS. W. F. PFEIFFER, Nederl. Tijdschr. v. Geneesk. **71**:190, 1927.

During an influenza epidemic a child, aged 2½ years, had fever and swollen backs of the hands and feet. The swelling increased and small hemorrhages developed on both hands and feet. These hemorrhages extended quickly, so that there were extensive blue-black hemorrhages with swelling and formation of blisters on the backs of the hands and feet; the same appeared on the auricles. In the region of these hemorrhages necrotic spots soon developed, and on some days both indices, thumbs and big toes were mummified. The next day the child died. "Per exclusionem" the diagnosis purpura fulminans was made, the symmetry of the bleedings being most striking and pointing to a condition of the center of vascular innervation.

THE ACRODYNIC SYNDROME. J. GOUDSMIT and H. C. RÜMKE, Nederl. Tijdschr. v. Geneesk. **71**:161, 1927; THE ILLNESS ACRODYNIA, "DERMATOPOLYNEURITIS," ERYTHREDEMIA, "VEGETATIVE NEUROSIS (= MORBUS) OF SWIFT-FEER. J. H. WIGGELENDAM and TACO KUIPER, Nederl. Tijdschr. v. Geneesk. **71**:250, 1927.

In the first article the authors describe in detail a case of the so-called vegetative neurosis of Swift-Feer in a girl, aged 9 years. They refer to the differential diagnostic difficulties and mention the conditions with which the disease may be confounded. In discussing the pathogenesis of this disease, known in literature under different names, the authors come to the conclusion that different causes may give rise to corresponding diseases (intestinal toxins, encephalitic toxins, etc). In their opinion the different cases described as Feer's disease or acrodynia do not form a nosologic unit. Feer's conception of the disease as a neurosis of the whole vegetative system is rejected. The authors believe that the "acrodynic syndrome" may be caused by a disease of the peripheral nervous system, diencephalon and mesencephalon. If only the vegetative nuclei are attacked, the clinical picture of the disease as described by Feer will develop; if only the mesencephalon and peripheral nervous system are attacked, conditions as described by the authors will develop.

In the second article Wiggelendam and Kuiper describe two cases of the disease, one in a girl, aged about 3 years, and one in a boy, aged 4 years, both of the same family. The girl died within a few months. The authors draw special attention to the neurologic symptoms which, in their opinion indicate that in this disease a condition of the central as well as of the vegetative nervous system may exist. The etiology would be infectious, perhaps the same as that of the encephalitis lethargica. They base this conception especially on the fact that two children of the same family became ill at the same time, and that the disease often begins with a condition in the nose and throat. Also the fact that at the same time that the children fell ill, a condition resembling mostly epidemic encephalitis occurred in the same village and even in the same family is given as an argument for the infectious conception of the disease. The authors regard the appearance of total exhaustion as a prevailing symptom of the disease. They are also of the opinion that the symptomatology of the disease depends on the extension of the condition in the central and vegetative nervous system. They propose the name of "vegetative syndrome of diencephalon and mesencephalon" for the disease. The boy was given a diet rich in vitamins, green vegetables, hydrotherapy and calcium. Within a few months he improved greatly.

Nervous Diseases

THE PATHOLOGY OF AMYOTONIA CONGENITA. ROY R. GRINKER, Arch. Neurol. & Psychiat. **18**:982 (Dec.) 1927.

A case was described that clinically belongs in the group of amyotonia congenita as originally described by Oppenheim. It belongs in this group because of the nonfamilial history, the onset of the disease during the first few months of life, if it is not congenital, and the diffuse muscular hypotonia without localized atrophy. The essential pathologic changes in the central nervous system were entirely within the confines of the lower motor neuron.

All the infantile degenerative muscular atrophies may be classed according to this pathologic criterion; namely, in one, a paucity of cells of the anterior horn with the presence of abnormal cells is found; in the other, actual degeneration of the ganglion cells and neuronophagia is seen. The first type is called Oppenheim, and the second is called Werdnig-Hoffman. There is no definite clinical differentiation between them, each type merging into the other.

SANFORD, Chicago.

THE USE OF ROSENOW'S SERUM IN THE TREATMENT OF INFANTILE PARALYSIS. FLOYD CLARKE, Nebraska M. J. **8**:428, 1927.

A recent case is cited in which a patient with infantile paralysis recovered with weakness of the left leg only. Rosenow's serum had been given three days before the onset of paralysis. In six other cases, the condition was diagnosed before the onset of paralysis and serum was given; this patient recovered without paralysis. The most reliable single diagnostic symptom is rigidity of the neck.

HAMILTON, Omaha.

TETANY OF THE SPHINCTER OF THE BLADDER. P. ROHMER and LOUIS GERY, Rev. franç. de pediat. **3**:533, 1927.

The authors describe a patient with spasm of the sphincter of the bladder which seemed to be linked with a severe spasmophilia of several years' duration. There was a temporary improvement in symptoms following the administration of parathyroid extract — Collip, but the child died about a week later of bronchopneumonia. The parathyroid glands showed nothing abnormal. Bilateral hydronephrosis was present. It is interesting to note that the existence of an acidosis, undoubtedly due to renal insufficiency, did not prevent the development of the symptoms and signs of tetany.

CARDIAC PHENOMENON IN SPASMOPHILIA. FELIX KLEIN, Rev. franç. de pediat. **3**:539, 1927.

While being fed from the bottle, an infant known to be spasmophilic suddenly showed a great increase in the intensity of the heart beat but no acceleration of the rate and no irregularity. The whole body of the infant was shaken by each contraction of the heart. This phenomenon disappeared with the administration of calcium chloride.

LESLIE, Chicago.

PAPILLOMA OF THE CHOROID PLEXUS. G. BUCCIARDI, Clin. Pediat. **9**:339 (April) 1927.

In two infants, aged 16 and 8 months, the condition was clinically diagnosed as congenital hydrocephalus. At autopsy, both showed the presence of voluminous papillomas in the lateral ventricles. Because of their macroscopic and histologic structure, the papillomas were not considered due merely to a hyperplasia of the ependymal cells, but as true tumors of the plexuses. In the pathogenesis of congenital hydrocephalus, it must be borne in mind that tumors of the brain, especially papillomas of the choroid plexus, may play

an important part, more frequently perhaps than is generally supposed. The hydrocephalus occurring in these cases as an accompaniment or sequel to the tumor is not always due to the accumulation of fluid incident to compression and venous stasis. It is due to a large extent to an active hypersecretion on the part of the epithelial cells in the villi of the papilloma. The excessive secretion of fluid is perhaps due to a superadded local irritative condition which occurs secondarily to the presence of the tumor. Under opportune conditions, many of these cases may be amenable to surgical intervention for the ablation of the tumor.

MENINGORADICULITIS. P. FORNARA, Clin. Pediat. **9**:403 (May) 1927.

A boy, aged 12 years, was suddenly taken ill with what appeared to be a mild febrile attack which progressed rapidly and reached its maximum within three or four days. The onset was associated with malaise and headache, and within a few days signs of meningeal irritation were observed (rigidity of the neck and positive Kernig, Lasegue and Brudzinski signs). The boy also had a complete paralysis of the two branches of the facial nerve and quadriplegia. The paralysis of the facial nerve was peripheral in type, and the paralysis of the limbs was flaccid with loss of all tendon and periosteal reflexes, rapid and marked amyotrophia. There were spontaneous pains in all muscles, and pressure over the larger nerve trunks elicited pain. The latter symptoms were apparently typical of polyneuritis, but the persistent signs of meningeal involvement, later verified by examination of the spinal fluid, led to the diagnosis of a craniospinal radiculitis associated with a diffuse meningitis.

The author was able to collect reports of fifteen similar cases in the literature. The onset is acute and is soon followed by paralysis of the limbs of the quadriplegic type, facial diplegia, abolition of tendon reflexes (cutaneous reflexes are retained), paresthesias, painful muscles, slight changes in the electrical reaction of the nerves and muscles and symptoms indicating a meningitis. The spinal fluid shows a hyperalbuminosis without cellular changes. The relationship between this syndrome and epidemic encephalitis still remains a disputed question. Various theories regarding its etiology have been propounded, but as yet it remains an unsolved problem.

MENINGITIS DUE TO THE PFEIFFER BACILLUS. R. DARDANI, Clin. Pediat. **9**:437 (May) 1927.

Meningitis caused by the Pfeiffer bacillus does not differ clinically from that caused by other organisms. In the present state of our knowledge, it is impossible to state definitely the relationship existing between the influenza organisms found in meningitis and those isolated from influenzal rhinopharyngitis.

In the author's case, the preexisting rhinitis and bronchopneumonia pointed to the fact that the meningitis was secondary.

ZAMBARANO, Northville, Mich.

EGGS IN THE DIET OF THE SPASMOPHILIC PATIENT. K. KLINKE, Jahrb. f. Kinderh. **114**:1 (Sept.) 1926.

From the literature summarized here, it is evident that in the administration of eggs to the spasmophilic patient, a rich supply of calcium must be furnished if edema is to be avoided. The increase of calcium was obtained by Klinke by adding from 1 to 2 Gm. of calcium carbonate for every egg or egg yolk. The necessary fat increase of the food is supplied by from 10 to 30 Gm. of roasted flour. A compound resembling breast milk was obtained by the use of thick (about 10 per cent) rice water. The preparation of the food is simple. The cooled rice water is added to the egg. Then the roasted flour and sugar as well as chalk are added. In most cases, 5 per cent more sugar is added. One gram of common salt is added to the finished food.

At the beginning of the treatment, 5 Gm. of calcium chloride is also given, but this medication is gradually decreased and stopped. After purging and a twelve hour interval during which tea is given (Teepause), thick rice water only is given throughout one day. At the same time, 5 Gm. of calcium chloride in the usual 20 : 300 solution p.d. is given. On the next day, one egg or egg yolk is whisked into the day's amount of rice water. Then from 2 to 3 Gm. of chalk is added. Within the next few days, a second egg or egg yolk is added with chalk and roasted flour. In this way, through increasing the flour and sugar, a food mixture with sufficient calories is reached which will be suitable for the child for some time. In forty-one of fifty-one spasmophilic children, this food was well supported. In the rest, it was impossible to continue the egg diet. The hypersensitiveness to electricity and other symptoms disappeared promptly in almost all cases. The edema which Bossert found to be provoked by the egg diet is safely avoided by the addition of calcium salts. The longest observation of the use of this diet was four months.

PACE, Chicago.

TREATMENT OF CHOREA WITH INJECTIONS. I. SOMOGYI, Orvosi hetil. **71**:547, 1927.

Intramuscular injections of milk with the usual technic were used in the treatment of about thirty patients with chorea. The results seem to be satisfactory. Improvement was noted two or three days after the first injection, and complete recovery in from three to five weeks. None of the patients treated by this method showed any recurrence of chorea. The same treatment was also used in the treatment of encephalitis, with satisfactory results.

THE FATE OF SUBSTANCES INJECTED INTO THE CEREBROSPINAL CANAL. G. JANOSSY, Orvosi hetil. **71**:674, 1927.

The author investigated the question whether certain drugs act on cerebrospinal centers more promptly through the circulation of the blood or through the cerebrospinal fluid. In the first series of his experiments, lobeline and atropine were used in intravenous and intraspinal form. In another series of experiments, he investigated whether the cerebrospinal fluid has any capacity to bind certain drugs. In this series, pilocarpine was used. The results showed that the cerebral centers are more easily affected by drugs through the circulation of the blood than through the cerebrospinal fluid. Certain substances will act more promptly through the cerebrospinal fluid, but only if they are injected in the vicinity of the center on which they have an elective action. The cerebrospinal fluid has no capacity to bind any drugs.

The substances injected in the cerebrospinal canal will only have an elective action on certain centers, but this action may be considerably different from that observed through intravenous or subcutaneous injections. Substances injected into the cistern may act on centers of the cerebrum. The passage of substances from the cerebrospinal fluid into the circulation of the blood is not as simple as it was thought before. Certain substances like atropine, epinephrine, nicotine, bacteria and certain oils will be retained for different lengths of time in the cerebrospinal fluid.

ZENTAY, St. Louis.

TOXIC MENINGITIS AND MENINGO-ENCEPHALITIS DUE TO ASCARIS INFESTATION. FELIX RAUDKEPP, Fol. Neurop. Eston. **6**:13, 1926.

Nervous symptoms are fairly frequently observed in cases of ascaris infestation. They begin suddenly and often resemble acute meningitis, particularly tuberculous, but the course is benign, and recovery follows the elimination of the worms.

The author reports a case in a girl, aged 7, who was somnolent and apathetic, and who suffered from headache and vomiting. There was weakness

of the left side of the face, of central character, with bilateral nystagmus and ptosis on the left side. The right and left muscles of the external rectus were also weak, the trunk was deviated to the left; there was dysphagia and nasal speech. Both arms and legs were weakened, and the tendon reflexes were increased, with positive Babinski sign and clonus. There was some salivation and subfebrile temperature. The spinal fluid was under increased pressure, clear, and contained a number of cells, with normal albumin. Culture and smear were negative. The nature of the condition was not suspected, and treatment was started with methenamine and mercury. The complaint of abdominal pain caused examination of the feces, and many ascaris ova were found. The child was removed from the hospital before treatment became effective, but was returned in a week practically unchanged. Further anthelmintic treatment was followed by the expulsion of a large number of worms, and from this moment the general condition of the patient became better, and the objective symptoms disappeared.

The theories as to the causation of nervous symptoms in ascariasis comprise reflex stimulation of the nerve endings in the intestinal tract and intoxication by the endogenous products of the worms. In animal experimentation such intoxication can be brought about by the injection of extract of ascarides. The changes in the cerebrospinal fluid certainly indicate the latter theory as the correct one. The reason that such intoxication does not take place oftener may possibly be due to the protective rôle played by the "barrier" of v. Monakov.

FREEMAN, Washington, D. C.

Diseases of the Eye

THRUSH OF THE CONJUNCTIVA. A. H. NORTON, Am. J. Ophth. **10**:357 (May) 1927.

A case report is given of a boy, aged 5, with thrush of the conjunctiva.

PHOTOGRAPHS OF THE FUNDUS OCULI, NORMAL AND PATHOLOGICAL CONDITIONS, WITH CASE HISTORIES, SINGLE AND STEREOSCOPIC VIEWS. ARTHUR J. BEDELL, New York State J. Med. **27**:951 (Sept. 1) 1927.

By means of the Nordenson camera, more than 600 eyes were examined. The various pathologic processes in the retina, choroid and optic nerve were photographed, and excellent pictures of the usual and unusual changes in the fundus were secured.

A number of the patients were children, the youngest aged 4 years.

Eight plates show more than 100 of the photographs obtained.

A photograph gives a permanent record of an exact reproduction of the object viewed. The method will be of great value in teaching and makes it possible to show the progress of many diseases. Pictures taken before and after operation for tumor of the brain will give a clearer conception of changes in the optic nerve.

AIKMAN, Rochester, N. Y.

EXPERIMENTAL CONGENITAL CATARACT. A. BAIVY, Arch. internat. de méd. exper., 1927, vol. 3.

The author presents the results of his experiments to test the work of Guyer and Smith on the production of congenital cataract, by injecting the gravid animal with anticrystallin prepared in the cock. Thirty young rabbits were obtained from six gravid ones thus treated. Two had opacity of the lens, which disappeared in a few days. Eight had small, weak eyes. One presented at autopsy a soft liquefied lens and one a definite cataract. No changes in the eyes occurred in the controls.

Baivy is undecided as to the mechanism — whether it is a precipitation in utero of the crystallin of the fetus by an anticrystallin in the blood of the

mother or whether, as Guyer and Smith believe, it is due to a destruction of the lens by cytolysins which accompany the precipitin prepared by the cock. Why it attacks the fetus and not the mother may be due to the fact that the lens of the fetus is more exposed to the blood stream in the hyaloid artery, which is not present in the adult.

A practical suggestion is made, namely, that it is inadvisable to operate for cataract in a pregnant woman because of the large amount of anticrystallin which might develop, as may occur after simple incision of the lens in rabbits.

N. ENZER.

Diseases of the Ear, Nose and Throat

OTITIS MEDIA IN INFANTS. DEAN M. LIERLE, Ann. Otol. Rhin. & Laryng. **36**:604, 1927.

A syndrome of intestinal disturbances produced by otitis media in infants has frequently been described during the past two or three years. This relationship has been observed and reported by many different otologists and pediatricians, who, in general, conclude that an otitis media may be accompanied by disturbances of nutrition as evidenced by dyspepsia and emaciation; that on evacuation of the contents of the middle ear, disturbances in digestion disappeared and an increase in weight followed; that elevations in temperature occurring with intestinal disturbances might be referred to complications of otitis, and that in all intestinal infections of infants accompanied by elevations in temperature and reduction in weight, an examination of the ears for the possible presence of otitis should not be neglected. Acute nutritional disturbances in infants, associated with diarrhea, fever, hydrolability and toxic symptoms are often not the result of intestinal infections or of food poisoning, and it is concluded that there must be some metabolic disturbance or a toxemia of an infectious nature.

Lierle reported a group of 100 cases examined and studied during a period of four years. He found that infections of the tympanum and mastoid are apparently secondary to infection in the nose and throat. A diagnosis of paranasal sinus disease was made in all but six cases of this series during the last two years. Ninety-two patients had involvement in both ears. Spontaneous rupture of the drum membrane occurred in twelve. The majority of the cases presented slight pathologic change in the drumhead. The luster was usually gone, and the membrane appeared dirty white, gray or a dirty yellow. Paracentesis frequently did not reveal pus or serum in the middle ear, but on opening the mastoid antrum a definite amount of pus was found often under much increased tension. The predominating organism in these cases was the hemolytic streptococcus.

Formerly, many of these infants died without being suspected of having any involvement in the ears or sinuses until it was disclosed at autopsy. The large numbers disclosed at autopsy is what has given impetus to the work on this subject in recent years. The prognosis depends on the duration and character of the infection, as well as on the presence of other systemic complications. The virulence of the organism is a large factor in the prognosis. The author makes a plea for the close cooperation between the otologist and the pediatrician in the handling of these cases, as acute otitis media in infants is rarely an otologic problem alone.

SNAPP, Grand Rapids, Mich.

PULMONARY ABSCESS FOLLOWING TONSILLECTOMY: PRELIMINARY REPORT. ALTON OCHSNER and WELLWOOD NESBIT, Arch. Otolaryng. **6**:330 (Oct.) 1927.

Three theories have been advanced concerning the routes for infection in the production of pulmonary abscess following tonsillectomy: (1) the lymphatic system, (2) the cardiovascular system and (3) the tracheobronchial tree. The first has been proved anatomically unsound. Experimental work on

dogs in which virulent organisms were introduced into the wound caused by the tonsillectomy showed infective emboli in the surrounding vessels, and cases have been reported in patients who had pulmonary abscess of definite embolic origin. Myerson found blood and pus in the trachea and bronchi in 155 of 200 patients on whom tonsillectomies had been performed under general anesthesia. It has been found that in abscesses of the lung following tonsillectomies, the various locations in the lung bear the same ratios as abscesses from aspirated foreign bodies. The fact that this complication may occur with local anesthesia was also shown. The anterior pillars of the pharynx of five patients were anesthetized with procaine and the patients told to swallow. All of the contrast substance (iodized oil) used in the test was seen fluoroscopically to pass directly into the tracheobronchial tree. It is reasonable to assume that infective material may likewise pass into the lungs during tonsillectomy under local anesthesia; this was found by Moore in 19.3 per cent of the patients examined.

Is Mastoidectomy Necessary in Young Children? Louis H. Schwartz, Arch. Otolaryng. **6**:353 (Oct.) 1927.

Because of the difference in structure, mastoiditis in the infant and small child is different from that found in the adult. At birth, the mastoid antrum is the only mastoid cell. This is fully developed and is often even larger than in the adult. The squamosal bone is separated from the mastoid process by the mastosquamosal suture, and pus from the middle ear and mastoid antrum may thus pass out to form a subperiosteal abscess over the mastoid process of the temporal bone. The vault of the tympanum is thin, and this, together with the free vascular supply between the space and the intracranial venous sinuses, makes meningeal symptoms common in even mild forms of acute otitis.

Treatment for mastoiditis in children should be conservative, as the dangers of operation and its complications are more serious than less radical procedures. The drum should be incised early and free drainage maintained, even if suction is necessary to promote it. Complications in the nose and throat should be cared for simultaneously. Though the hearing is temporarily affected, it does not remain so.

Septicemia of Otitic Origin Via the Jugular Bulb: Report of a Case. Edward R. Roberts, Arch. Otolaryng. **6**:383 (Oct.) 1927).

A patient with septicemia of acute suppurative otitic origin is described in whose case a diagnosis was made with the usual certainty but who recovered without any further operative procedure than a myringectomy. There was no evidence of mastoid involvement, and it is assumed that direct infection of the bulb took place, either without the formation of a thrombus or with the formation of such a thrombus that surgical intervention was not required.

Barnett, Chicago.

A Case of Acute Osteomyelitis of the Superior Maxilla with a Large Infra-Orbital Abscess in a Nursing Infant. Gino Merelli, Rev. Oto-Neuro-Oftalmologica **4**:435 (July-Aug.) 1927.

Merelli reports a case of an infant, aged 3⅓ months, who showed an enormous edema of the right lower eyelid of rapid onset. The mother said that for three days, without any known reason, the infant had refused food, vomited and had diarrhea. At the same time, the swelling was noticed.

General physical examination gave negative results, aside from an acute inflammation of the gastro-intestinal apparatus. External examination of the face showed that the right lower eyelid was reddened and edematous, so as to close the palpebral cleft completely. Palpation gave a sense of fluctuation, more especially toward the external part of the orbit. The right cheek, showed a swelling and redness corresponding with that of the upper part,

though in less degree. Signs of acute inflammatory process were not seen in the nose. A marked painful swelling was found in the mouth; in the zone corresponding to the hard palate on the right side was a fistula from which came pus and in which a probe was passed for several centimeters against necrotic bony tissue on the right alveolar margin. A diagnosis was made of acute osteomyelitis of the superior maxilla.

Operation was done under local anesthesia through a deep incision in the gingivobuccal fold, with drainage and packing. The postoperative course was good, and the symptoms rapidly subsided. The fistula closed.

Merelli states that acute osteomyelitis of the superior maxilla in nursing infants and in the new-born is rare.

In discussing this case, Merelli states that the initial diagnosis is difficult, but that later the condition gives a characteristic triad: (1) swelling of the cheek of the alveolar margin and that side of the palate, (2) the presence of superficial abscesses and fistula in characteristic points and (3) expulsion, also spontaneous, of tooth buds and bony sequestrums.

The author mentions the importance of differentiating this condition from phlegmon of the orbit, from purulent ophthalmia and from dacryocystitis. He says that the prognosis is always grave because the mortality is often serious, going from 30 to 50 per cent. Septicemia with purulent visceral localization is always a frequent complication. In the most benign forms, the process tends to become chronic and the suppuration continues for months.

Cases like the author's in which complete cure comes on quickly, are rare.

In regard to operative intervention, which must always be early, Broca distinguishes the cases in which fistulization has occurred and those in which it has not occurred. In the cases in which fistula exists, Broca advises cleaning up the abscess and taking away the sequestrums and granulations to give ample drainage. On the other hand, in any case in which fistulization has not occurred, the incisions usually made across the cheek are contraindicated on account of the deformities and those through the nasal cavity are also contraindicated because they are dangerous and difficult to perform in infants. The point of election in which to reach the various places of infection is the gingivobuccal sulcus. One of the most important principles of general operations in osteomyelitis is that of opening the various zones of infection, as much as possible.

Diseases of the Skin

PEMPHIGUS IN A CHILD. E. A. MORGAN, Canad. M. A. J. **17**:1040, 1927.

The case reported is chiefly of interest because of its severity and because of the fact that the girl has been free from symptoms for seven months. In a girl, aged 13 years, the first appearance of the pemphigus was a bleb about the size of a quarter on the buccal mucous membrane inside of the lip. There was a rapid extension of the condition over the mucous membrane of the mouth and nose and over the conjunctiva. Blebs did not appear on the skin at any time.

Treatment consisted of frequent douching with large amounts of dilute lavoris or baking soda solution followed by the application of a solution of 2 per cent mercurochrome-220 soluble.

Recovery was complete in three or four weeks without visible scarring in the mouth.

MOORE, Chicago.

SOME PRACTICAL POINTS IN THE TREATMENT OF RINGWORM WITH THALLIUM. J. H. TWISTON DAVIES, Brit. J. Child. Dis. **24**:219 (July-Sept.) 1927.

Thallium has a unique action on the hair of the scalp as well as on the sympathetic nervous system, according to the author. Most animals, except the guinea-pig, shed their hair when thallium is administered in a certain dosage; any smaller dosage definitely increases the rate of growth. The therapeutic defluvium is preceded by a visible increase in the rate of growth.

The technic consists of the administration of thallium acetate, 8.75 mg. per kilogram of body weight given in a little sugar and water, the solution being freshly prepared from fresh salt. All hats, towels, etc., are disinfected. A cotton skull cap is worn constantly and is changed several times a day. The hair is cut to about ½ inch length. The head is washed on alternate days for six days, then daily. All of the scalp except the infected areas is rubbed with Whitfield's ointment daily after the shampoo.

The child comes for inspection immediately if the hair is found to be loose (usually from the seventh to the seventeenth day). Healthy hairs around the infected patches are then plucked till a ring has been cleared; the infected hairs are extracted with lens and forceps, and the patches painted with 4 per cent tincture of iodine for four days. When the whole scalp is bald, tincture of iodine is applied over its entire surface and Whitfield's or sulphur ointment administered. This treatment is continued for three weeks, i. e., iodine and ointment.

LANGMANN, New York.

ENDOTHELIOMA IN AN INFANT. ERIC I. LLOYD, Brit. J. Dermat. **39**:289 (July) 1927.

A case is described in a boy, aged 15 months, who at birth presented a small, hard, white spot in the left suprascapular region that gradually increased in size until the last few months, when it progressed rapidly. Local excision was performed, and the sections were diagnosed as probable endothelioma. An enlarged axillary lymph gland removed later showed metastases similar to the original tumor.

RECURRENT ONYCHOPTOSIS OCCURRING AS A FAMILY DISORDER. W. J. OLIVER, Brit. J. Dermat. **39**:297 (July) 1927.

Three cases are reported, the first one being observed by the author, and the notes on the other two being supplied by the parents. The first case is that of a healthy boy, aged 12, whose big toenail was involved and the second case is that of the boy's father, aged 42, who first shed his great toe-nail at the age of 36, and then annually for three years. In the third case, the brother, aged 14, shed both toe-nails when 12 years of age. Reference is made to cases reported by Montgomery and by Hutchinson.

XANTHOMATOSIS CUTIS AND HYPERCHOLESTEROLEMIA. J. T. INGRAM, Brit. J. Dermat. **39**:335 (Aug.-Sept.) 1927.

Ingram reviews the literature on blood cholesterol in xanthomatosis and on the pathogenesis of hypercholesterolemia and gives a detailed report of a girl, aged 11. The effect of insulin in hypercholesterolemia is discussed. The patient had xanthoma tuberosum with deposits in the tendons and a blood cholesterol of 430 mg. per hundred cubic centimeters. There is a description of microscopic sections of the tumor masses that were excised. There was no apparent abnormality of hepatic, pancreatic or renal function. The blood cholesterol was not affected by administration of insulin. The author suggests that hypercholesterolemia in this case was due to a primary metabolic disorder. Treatment of the patient followed the lines of local applications, general measures having failed.

THE DETECTION OF RINGWORM HAIRS ON THE SCALP BY THEIR FLUORESCENCE UNDER ULTRA-VIOLET LIGHT. A. C. ROXBURGH, Brit. J. Dermat. **39**:351 (Aug.-Sept.) 1927.

This method consists of examining the head in a darkened room by the light from a mercury vapor or tungsten arc lamp passed through a piece of Wood's glass. Wood's glass is dark violet and contains oxide of nickel. It allows

only a little red and visible violet and some long ultraviolet rays to pass. Normal hair and skin show slight fluorescence under this light, the finger-nails react more brightly, but hairs infected with ringworm give a brilliant fluorescence with a greenish light. This enables one easily to identify small groups of infected hairs or even single stumps on an otherwise healthy scalp. The appearance becomes pathognomonic only when the hairs are infected. The author finds the method of value in ascertaining whether epilation after thalium acetate or roentgen-ray treatment is complete, or whether a few ringworm stumps still remain; it is also of value in deciding whether the brother or sister of a patient with ringworm is infected.

WIEN, Chicago.

INFANTILE ACRODYNIA. T. KUIPER, Presse. méd. **71**:1075 (Sept. 3) 1927.

From a study of a recent epidemic in Holland, Kuiper believes that the characteristic signs of acrodynia, namely, "raw beef" hands and feet, desquamation, perspiration and paresthesia, are all signs of a central disorder. The usual prostration that accompanies these signs is also a result of this disorder. Kuiper therefore advocates that acrodynia be named a syndrome of the vegetative nervous system.

SANFORD, Chicago.

CHRONIC TRICHOPHYTOSIS OF THE SKIN AND NAILS IN ALL MEMBERS OF A FAMILY, WITH INVASION OF THE MUCOSAE, LYMPH NODES AND BONE. A. PELÉVINE and N. TCHERNOGOUBOFF, Ann. de dermat. et syph. **8**:403 (July) 1927.

In a mother, two sons and a daughter, the nails were infected, and in the children wide areas of the skin were involved. In one there was granuloma formation, and sinuses were found leading to foci of infected bone; infected lymph nodes were present. In the daughter the organism was recovered from the vagina, and in one son the oral mucosa was infected. The children's nails had been infected soon after birth, the appearance of the generalized cutaneous involvement having been delayed. The nails were considered to have been the means of spreading the infection. A vaccine acted favorably.

PAROXYSMAL ACRODYNIA OF INFANCY. PIERRE BÉZY, Ann. de dermat. et syph. **8**:425 (July) 1927.

A typical case of acrodynia is described in a child, aged 4 years.

PARKHURST, Toledo, Ohio.

TREATMENT OF LEINER'S DESQUAMATIVE ERYTHRODERMIA WITH INJECTION OF MOTHER'S BLOOD. ZOLTAN V. BARABÁS, Jahrb. f. Kinderh. **112**:46 (March) 1926.

Barabás has used mother's blood in fifteen cases with good results in eight cases. Injection was followed in these cases by gain in weight, improvement in the skin eruption and also in the intestine. These injections were given in from three to five day intervals with from 6 to 10 cc. at each dose in from five to ten injections given into the gluteal muscles. Whether this causes a detoxication or adds vitamin are questions to be considered.

No conclusions are drawn.

EHRMANN, Chicago.

Surgery and Orthopedics

SURGICAL ASPECTS OF LUNG ABSCESS. GEORGE P. MULLER, Am. J. Roentgenol. **15**:421 (May) 1926.

The author cites several series of cases showing the infrequency of pneumonia and bronchopneumonia as an etiologic factor in abscess of the lung. A great number follow operations on the upper respiratory passages, possibly 50 per cent and as high as 75 per cent following tonsillectomy. There is a

controversy as to the effect of motor driven anesthesia apparatus, but a number of cases have followed local anesthetic. Dislodging of septic thrombi formed in the throat may produce the abscess. The treatment consists of adequate drainage. This may be accomplished by postural drainage, bronchoscopic aspiration, the production of artificial pneumothorax and external drainage by thoracotomy. The surgeon is greatly aided by an anteroposterior stereoscopic study and lateral views. An old abscess with thick walls and the presence of pleuritic adhesions are a contraindication to artificial pneumothorax. The principal objection to surgical intervention is the high mortality; different series show a mortality ranging from 20 to 35 per cent. Lord reports 11 per cent recovery in patients not operated on which lasted over two months but estimates that persistent medical treatment would result in a mortality of 75 per cent. Local anesthesia and preferably a two stage operation with rib resection as the first stage are recommended. At the second stage, after localization, either lobectomy, partial excision or cautery pneumectomy is done by various surgeons.

STULIK, Chicago.

JOINT AND BONE INFECTIONS IN CHILDREN. JAMES S. STONE, Boston M. & S. J. **197**:507 (Sept. 29) 1927.

Provision for growth in the length of bone at the epiphyseal line in children tends to protect the surfaces of the joints by diverting fractures at this weak point, but increases the likelihood of injury to the bone with subsequent infection.

Epiphyseal separation is common but not always demonstrable in the roentgenogram. Clinical history and observation are therefore important. Localized tenderness about the epiphyseal line, impairment of function and a consistent history are factors necessary for diagnosis. Subperiosteal (greenstick) fractures are common in children. Localized tenderness, particularly encircling the bone, an impairment of function and a consistent history are important clinical factors in the absence of deformity, crepitus or abnormal mobility. Roentgenograms are often negative if taken in only one plane.

The great liability to minor injury and slight hemorrhage at the epiphyseal line renders this area peculiarly susceptible to infection, if the resistance is lowered and if there is a primary focus from which the infection may start, such as umbilical infections in the new-born, pneumonia, infected blisters, boils and tonsils. The infection may spread backward into the medullary cavity, causing true osteomyelitis, especially in older children, or in younger children the infection may originate away from the epiphyseal line and may not involve the shaft. The treatment is adequate drainage. The abscess may involve the joint or only the soft tissues, but "the pus should be followed and let out no matter where it leads the operator."

Infantile scurvy is becoming less common as fruit juices are included in the diet. Epiphyseal and periosteal lesions are among the most characteristic symptoms in this disease, causing pain on motion. "Hemorrhage under the gums is simply a visible subperiosteal hemorrhage."

Congenital syphilis also involves the epiphyseal lines which pathologically are characterized by a yellowish color, increased breadth and slight irregularity. The clinical symptoms of tenderness, swelling and unwillingness to use the limbs suggest scurvy but are less severe.

Tuberculous infection in bone is apt to involve the epiphysis rather than the end of the shaft. The process is usually insidious in onset, slow in progress, and associated with considerable destruction and comparatively little proliferation of bone.

"Rickets notoriously causes marked changes at the epiphyseal lines but unless the degree of rickets is extreme or complicated by scurvy or an infectious process there is little if any risk of confusion in diagnosis."

Since the roentgen ray does not show a pyogenic infection of the bone until marked destruction has occurred or until sufficient time has elapsed for new periosteal bone to be formed, roentgenograms can be interpreted properly only in the light of a faithful history and accurate clinical examination.

GENGENBACH.

INDICATIONS FOR OPERATION IN HERNIA IN THE INFANT AND YOUNG CHILD. ANDRE MARTIN, M. J. & Record **126**:297 (Sept. 7) 1927.

1. In original hernia in which there is simple persistence of the peritoneovaginal canal, operation should not be performed until the fifth or sixth year. When the sac is usually reducible, operation should be performed toward the end of the first year.

2. When the sac is irreducible, operation should be performed in the absence of any general contraindication.

3. In umbilical hernia, operation should be performed about the fifth year.

4. In crural and epigastric hernia, operation should be performed as soon as the diagnosis has been determined.

WILLIAMSON, New Orleans.

DYSENTERY AND APPENDICOSTOMY. W. T. RITCHIE, Edinburgh M. J., Tr. Medico-Chir. Soc. Edinburgh **34**:144 (Aug.) 1927.

Appendicostomy apparently cured a case of dysentery in a girl, aged 14, who was sick for three weeks. The causative micro-organism was not proved although amebas of the *Entameba coli* type as well as other organisms were found at different periods.

NEFF, Kansas City, Mo.

ENCEPHALOCELE: THE ANATOMIC STUDY AND SURGICAL TREATMENT IN FOUR CASES. J. PIRQUET and R. TRAMBLIN, Arch. franco-belges de chir. **29**:945, 1926.

Defects in closure of the neural tube at the cephalic extremity are divided anatomically into meningocele, encephalocele, encephalomeningocele and encephalocystocele, depending on the degree of prolapse of the intracranial contents. Most of these defects develop at the craniospinal junction, although some are found in the ethmoid region and may be even orbital or intranasal in location.

The treatment of encephalocele has undergone improvement recently, although until early in this century operation was rarely practised. The operation is best performed as early as possible in order to avoid the advent of ulceration and infection. When the encephalomeningocele is large and associated with cranioschisis, operation is of no use; if there is serious malformation of the skull or a fissure involving the foramen magnum and the spine, operation should be refused. Large cranial openings, if operated on, usually terminate in hydrocephalus, and hydrocephalus itself is a contraindication. Only children in good general condition should be operated on, and in those showing manifest infection in the eyes, ears or skin, operation should be avoided.

The classic operation consists of dissection of the cutaneous coverings, ligation of the pedicle and puncture of the sac. This is followed by extirpation of the pedicle and reduction of the herniated cerebral tissue, the escape of cerebrospinal fluid, being avoided, if possible; the cranial gap is closed by fibrous tissue in the pericranium before suture of the skin. The authors believe that it is not necessary to open the cyst or reduce the herniated parts of the brain. Drainage does not seem to be necessary. Escape of cerebrospinal fluid often leads to collapse and should be avoided if possible. A flap may be necessary to close the skin; it is sometimes more difficult to close the osseous breach. The danger of infection is not great if infection does not exist at the time of operation. Among the latter results, hydrocephalus is unfortunately frequent but can be handled fairly well by repeated lumbar punctures.

FREEMAN, Washington, D. C.

A Case of Osteomyelitis of the Cervical Spine with Cerebrospinal Symptoms. Felix Basch, Jahrb. f. Kinderh. **112**:51 (March) 1926.

A boy, aged 13, had pain in the neck and between the shoulders, fever and chills, nausea, headache, rigidity of the neck, normal sensorium, unequal pupils, motor weakness of the left arm, hyperesthesia of the left hip and a positive Kernig sign. Lumbar puncture showed: clear spinal fluid; normal pressure; Pandy +++; 17 cells per cubic millimeter. On the following day, hyperesthesia of the first third of the left forearm and hyperesthesia on the ulnar surface with exaggerated knee reflexes were found. These symptoms suggested a lesion in the region between the cervical and dorsal spine. At operation, an abscess the size of a walnut was found to the left of the seventh cervical spine and a smaller one to the right of the spine. Recovery followed, with permanent paralysis of the left hand.

Ehrmann, Chicago.

Miscellaneous

Roentgen Treatment of Spontaneous, Posttraumatic and Postoperative Coccus Infections and Suppurations. Holzknecht, Am. J. Roentgenol. **15**:332 (April) 1926.

Timely and correct administration of roentgen rays produces a favorable termination in a majority of patients with acute or subacute coccus infections of all regions. The effect is judged by (1) pronounced recession of the infiltration and swelling in from one to four days following a slight increase lasting half a day or (2) by cessation of general symptoms except temperature. In pneumonia, there is improvement in the respiration and in the heart. The technic is partly roentgenotherapeutic and partly combined with surgery. Radiation of medium penetration through 0.5 mm. heavy metal, applied over the infected focus and its immediate surroundings with a surface dose of about 20 per cent of the skin unit dose (equal 2 Holzknecht units) should be administered early. In the most acute conditions, 1 Holzknecht unit should be applied, and for children from ½ to ¾ Holzknecht units is recommended. The result is a four to six day increase in the bacteriolytic power of the blood. Sterile pus is frequent after irradiation. According to Pordes, there is injury of the highly sensitive leukocytes in the inflammatory area followed by a release of the antitoxins and bacteriolysins which they contain by virtue of constitutional and pathologic factors.

Stulik, Chicago.

Suggested Nomenclature for Ultraviolet Zones. Herman Goodman, Arch. Dermat. & Syph. **16**:3 (Sept.) 1927.

The author's divisions of ultraviolet rays into regions and the nomenclature thereof are based on physiologic responses, especially by the skin. The "intravital" ultraviolet zone is from 390 millimicrons, the lower limit of visible light, to 320 millimicrons, the conventional barrier of glass to ultraviolet rays. The "vital" ultraviolet zone is from 320 to 290 millimicrons, the limit of natural sunlight. The "extra vital" zone is from 290 to 200 millimicrons, the limit of penetrability of air.

Jeans, Iowa City.

The Bactericidal Activity of Hexylresorcinol in Glycerin. Veader Leonard and William A. Feiber, Bull. Johns Hopkins Hosp. **41**:21 (July) 1927.

The authors think that "disinfection by chemical means is an orderly time process, exhibiting all of the mathematical characteristics of a chemical reaction of the first order—a so-called unimolecular reaction—such as the hydrolysis of cane sugar. The velocity of such a reaction as well as its completeness is influenced, just as chemical disinfection is influenced, by four physical factors, namely, concentration, temperature, pressure and time."

With the cell protoplasm as one reagent and the disinfecting substance as the other, a reaction can occur only after the germicide has penetrated the cell membrane. To test the speed and completeness of this reaction, a series of experiments were carried out with special reference to the relations of surface tension and the effectiveness of hexylresorcinol. Fifteen of the common pathogenic organisms were used.

The authors conclude that surface forces play a major rôle in disinfection by chemical means. "A solution containing 30 per cent glycerin and 70 per cent water in which is dissolved 1 mg. of hexylresorcinol per cubic centimeter (1 to 1,000) possesses a surface tension of 37 dynes per centimeter (Solution S. T. 37) and appears to represent the optimal composition for clinical application in tissue surface disinfection, for the following reasons:

a. It is nontoxic and nonirritating.

b. The hexylresorcinol is held in perfect solution in all dilutions.

c. The surface tension is very low.

d. All the major types of pathogenic micro-organisms are destroyed in less than 15 seconds on contact with this solution.

e. Its bactericidal activity is retained (15-second standard) under all conditions of dilution likely to be encountered in clinical application as well as in the presence of organic matter."

LYTTLE, New York.

THE MALNOURISHED CHILD. L. W. SAUER, J. A. M. A. **89**:931 (Sept. 17) 1927.

The author outlined an individual intensive method of treatment of the malnourished child. In thirty consecutive cases reported, the average gain in three months was more than 11 pounds (5 Kg.), or five times the average rate of gain. Coincident with the increase in weight, there was usually marked improvement or disappearance of the pathologic condition.

BONAR, Salt Lake City.

RICKETS. W. W. ANDERSON, J. M. A. Georgia **16**:298, 1927.

Anderson discusses the etiology, prevention, symptoms, diagnosis and treatment of rickets. The value of diet, cod liver oil and violet ray in prevention and treatment is carefully considered.

THE USE OF BANANA DIET IN THE TREATMENT OF INTESTINAL INDIGESTION IN CHILDREN. JOSEPH YAMPOLSKY, J. M. A. Georgia **16**:302, 1927.

The author states that bananas, when ripe, are digestible. They were used in conjunction with protein milk and a regular course of intestinal elimination in three cases of severe celiac disease. The patients gained in weight and after two years of observation are apparently well.

STARVATION DIET VERSUS FEEDING IN THE TREATMENT OF SUMMER DIARRHEAS. W. A. MULHERIN, J. M. A. Georgia **16**:305, 1927.

Mulherin states that the modern idea in the treatment of ileocolitis is the same in principle as the treatment of typhoid fever—the infant's vital force should be supported with food of sufficient strength to be of some real value, until the infection has run its course. Symptoms should be treated as they arise, medicine being given only if there is a direct indication for it. Plenty of water should be given to drink; if necessary this should be forced or given artificially, in order to keep the tissues and organs of the body functioning in a normal manner, thereby preventing metabolic disturbances that frequently claim the life of the patient.

MASHBURN, Atlanta.

CLINICAL USE OF EPHEDRINE. W. S. THOMAS, New York State J. Med. **27**:831 (Aug. 1) 1927.

Thomas reports his clinical experience with ephedrine in 300 patients with asthma and hay-fever. He prefers the hydrochloride of ephedrine. He has not noted any ill effects or a tendency for the patients to form the habit of taking the drug. The proper oral dosage varies considerably in different persons of the same weight. Infants and children take ephedrine well, and it has been found effective in the relief of asthma in children. In hay-fever, better results are obtained when the drug is used both by mouth and locally in the nose.

CORRECTION OF PHYSICAL DEFECTS IN SCHOOL CHILDREN. FREDERICK W. SEARS, New York State J. Med. **27**:1081 (Oct. 1) 1927.

While medical examinations in the schools are progressing satisfactorily in cities and larger villages, the conditions in rural schools are, in most instances, deplorable. Nursing service was provided by the Onondaga Health Association in an attempt to demonstrate that such service would make physical examinations more satisfactory and by follow-up work to have recommendations carried out. The usual physical examinations were made by a school physician assisted by the nurse. The children's clothing was removed down to the waist line. In twenty small one and two room schools, 872 children were examined and 1,084 defects found. Within the first year 26 per cent of the defects in vision were corrected and 55 per cent of dental corrections made. Many diseased tonsils were removed, and conditions in the homes and schools were improved.

Toxin-antitoxin was given to nearly all the school and preschool children in the school districts.

As a result of the demonstration, the board of supervisors of the county appointed four additional nurses.

AIKMAN, Rochester, N. Y.

QUARTZ LIGHT AND DIATHERMY: THEIR PRACTICAL USE. A. L. GLEASON, Northwest Med. **26**:457 (Sept.) 1927.

Gleason believes that the quartz light has a limited field of usefulness. He quotes certain authorities as considering it far inferior to sunshine in tuberculous conditions. In dermatologic practice, the quartz light may clear some conditions, but may irritate acute dermatitides and stimulate a malignant condition. In rickets, the lamp is specific. The use of the lamp is hindered by the impossibility of accurately controlling dosage, as burners vary in intensity and skins vary in susceptibility. Irradiation of food may add antirachitic value to it but destroys vitamin A in milk. Glass permitting passage of the ultraviolet rays is being introduced and may supplant the quartz light to some extent. Diathermy produces heat that is nondestructive to tissue and is controlled by the size and position of the electrodes and by the strength of current. The results are good in neuritis, spastic torticollis and recurrent pleurisy. Its dangers are the absorption of toxic substances from the treated tissue and the possibility of hemorrhage from the severe hyperemia.

SCOTT, Philadelphia.

CEREAL FOOD: THEIR ADVANTAGES AND DANGERS. WESTON WILLIAM, Southern M. J. **20**:765, 1927.

A comparative analysis of the nutritive value and the minerals, iodine and vitamin content of wheat, oats, yellow corn and rice is presented. The author has used a food composed of 15 per cent yellow corn, 35 per cent wheat, 25 per cent oats and 25 per cent brown rice, and finds this combination of the cereals to exert the most favorable influence on weight and changes in the blood.

Cereals, as represented by grape nuts and corn flakes, possess so little value that their use should be abandoned.

SCHLUTZ, Minneapolis.

THE EFFECT OF CALCIUM IN CHILDREN. LEONARD G. PARSONS, Brit. M. J. **2**:780, 1927.

This is part of a detailed discussion regarding the therapeutics of calcium, in which the author speaks from the pediatric point of view. A review of the current opinions is presented, while his conclusions in regard to calcium therapy are to the effect that the chief employment is to be found in the relief of tetany. In all cases he concludes that adequate calcium is supplied in the food. However, in cases of spasmophilia due to alkalosis, the methods used to alter the blood reaction and thereby increase the ionic calcium are to give saline solution intravenously, to operate at once in cases of pyloric stenosis and to fill the abdomen with normal saline solution: after operation, the method is to feed the infant on lactic acid milk, if breast milk is unobtainable, in order to prevent the drain on the body chlorine ions caused by the high buffer value of cow's milk and the necessarily greater amount of hydrochloric acid required for peptic digestion.

BROWN, Toronto.

THE ACTION OF URINARY ANTISEPTICS. RALPH STOCKMAN, Edinburgh M. J. **34**:396 (July) 1927.

Professor Stockman, of the Department of Materia Medica and Therapeutics, University of Glasgow, discusses the action and value of the usual drugs given for rendering the urine antiseptic in infections of the urinary tract. He agrees that as yet there is not a perfect or powerful urinary antiseptic, something that is especially needed for treating children. Among the drugs discussed is first, acid sodium phosphate and its effect on the total acidity and on the hydrogen ion concentration of the urine. He believes that if the urine has been of low acidity or slightly alkaline that the sodium salt with hexamine permits the splitting off of a larger amount of formaldehyde than otherwise. When the urine is already acid, the use of acid sodium phosphate is unnecessary. He has found it difficult in some cases of alkaline or low acidity to raise the total acidity by giving 40 grains (2.6 Gm.) four times daily.

Benzoic acid and the benzoates have little action against an infection with *Bacillus coli*. Salol has little value as an antiseptic. In the opinion of Stockman, infection is not cleared up by the use of acriflavine or hexylresorcinol.

Stockman believes that boric acid is of benefit whether the urine is acid or alkaline. In *B. coli* pyelitis of children, it may be administered with the alkaline treatment, adding a valuable antiseptic element thereto. He would use bicarbonate of soda simultaneously with potassium citrate, as less disturbing to the stomach than either alone, and the alkalinity of the urine is more steadily maintained. Ten grains (0.65 Gm.) of boric acid with sodium or potassium citrate is soluble in one half ounce of water, but a larger dose should have a teaspoonful of glycerin added. With an acid urine Stockman believes that a combination of 10 grains of hexamine, 10 grains of boric acid, and 20 grains (1.3 Gm.) of ammonium benzoate in one-half ounce of water makes the most powerful urinary antiseptic that he knows.

NEFF, Kansas City, Mo.

PROGNOSIS IN ATHREPSIA. L. M. JANSEN, Nourrisson **14**:377 (NOV.) 1926.

In 1904, Quest claimed that a fatal prognosis can be made in cases of athrepsia when the weight of such an infant is reduced by a third or more over what it had formerly attained.

In a study of 176 athreptic infants who weighed less than two thirds of the weight normal for their age, Janset reported a mortality of only 58. On the contrary, in 236 infants who showed a loss in weight less than one third there were 21 who failed to survive. Therefore, the contention of Quest that the outcome in states of denutrition can be prognosticated from percentage of weight loss alone is not verified.

MCCLELLAND, Cleveland.

Is There Need for an Inquiry Into the Causes of Infant Mortality (in India)? Rao B. Shikhare, Rev. internat. de l'enf. **4**:583, 1927.

Answering the question in the affirmative, this Indian author quotes some appalling statistics for 1923, the latest available reports from the British foreign office. The total of births registered in that year were 8,466,085, a ratio of 35 per 1,000. The total deaths were 6,036,931, a rate of 25 per 1,000. The mortality among infants under one year was 1,486,277, or 24.6 per cent of the total. This gives an approximate death rate of 176 per 1,000, but examination of the reports from the larger cities shows a much higher loss even than this, Karachi having a death rate of 218; Madras, 254, and Poona, a rate of 592 per 1,000.

Of these infant deaths, 50 per cent occurred during the first month of life, and among this group 65 per cent died during the first week. It is apparent therefore that about 33 per cent of the total mortality in infancy may be assessed to factors affecting the newly born. Among the causes for this veritable slaughter of the innocents, Shikhare mentions the usual ones — ignorance, poverty, neglect, filthy midwives, hereditary customs and practices — prevailing in practically all primitive countries, and stresses one peculiar to India — the iniquitous practice of child marriage.

He urges the institution of those measures, such as infant welfare stations, training of midwives and education in sanitation, which have reduced the rate of infant mortality so strikingly in more fortunate lands.

Amesse, Denver.

The Effect of Certain Diuretics on Infants. Walter Baumecker, Monatschr. f. Kinderh. **36**:193, 1927.

In view of the importance of the work, the author repeated the experiments of Stransky and others, who investigated the effects of a certain number of diuretics on infants. The previous investigators had studied urea and the purin derivatives. This study includes merbaphen.

In regard to urea, the effect was somewhat inconstant. At times, it caused a marked diuresis. At other times, it was without effect. The success depended first on the dosage and second, on the type of child. The dosage was large and had to be repeated five or six times daily in amounts of from 1 to 2.5 Gm. Diuresis occurred in the child whose water excretion seemed of the extrarenal type. In the child whose excretion was purely renal, urea was without effect.

Merbaphen proved valueless in the normal child.

Theophylline sodio-acetate in doses of three times 0.05 Gm. caused a much greater excretion of water and chloride than did caffein and theobromin. The effect of these drugs is temporary and not so long as that of urea.

The Influence of Acidity on the Activity of Atropine and Homatropine. Helmut Mommsen, Monatschr. f. Kinderh. **36**:339, 1927.

There is no question but that the amount of buffer substance in a solution influences the activity of atropine. Tadpoles die in alkaline solutions of atropine and homatropine much more quickly than in acid solutions. The effects of these drugs on the widening of the pupils and toxic erythema of the skin is likewise much more active in the alkaline than in the acid. Perhaps the high tolerance of infants to atropine in pylorospasm is due to increased gastric acidity.

Gerstley, Chicago.

Society Transactions

NORTHWESTERN PEDIATRIC SOCIETY

July 16, 1927

H. F. HELMHOLZ, M.D., *Presiding*

THE INCIDENCE OF TUBERCULOUS INFECTION IN CHILDREN FROM RURAL DISTRICTS. DR. R. E. VORIES.

A tuberculin test is a routine procedure in the examination of all children seen in the Pediatric Section of the Mayo Clinic. The data for this paper were collected from a study of the histories of 1,000 children between the ages of 6 months and 15 years, who lived in communities with populations of less than 25,000 and who came from thirty-five states and from Porto Rico, Cuba, Mexico and Canada. All cases presenting evidence of an active tuberculous lesion were excluded.

In the 1,000 cases, 169, or 16.9 per cent, showed positive reactions. There was a striking increase in the number of positive reactions with an increase in age. There was a slightly higher percentage of positive reactions among the girls. Positive tuberculin reactions appeared to be of more significance in underweight than in overweight children.

A history of known contact was found in from 8 to 10 per cent of the patients with positive tuberculin reactions, and from 19 to 20 per cent gave a family history of tuberculosis. Of the 1,000 patients, 124 gave a history of tuberculosis in the family, with no known contact. There were 26.6 per cent of the positive reactions among the boys of this group and 26.5 per cent of the positive reactions among the girls.

In 144 cases, there were some evidences of the changes in the lungs by roentgen-ray examinations. Of these, 21.3 per cent of the positive reactions were found in boys and 28.9 per cent in girls.

The percentage of positive reactions compares closely with those obtained by Slater and Green and Forbes.

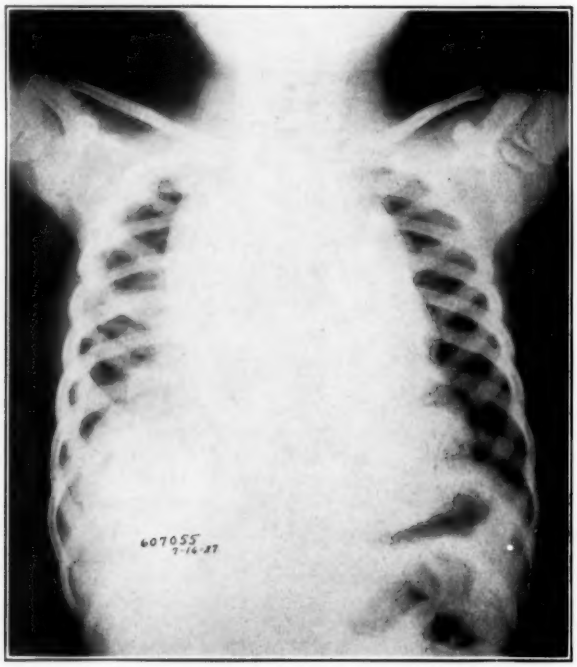
DISCUSSION

DR. JEANS, Iowa City: One of our group has recently gone over our records in regard to the same point. The figures obtained were similar to those just reported. We took children up to 15 years of age. In the group aged from 13 to 15, we found approximately 30 per cent positive reactions. This is a little higher than the 24 per cent recorded for the younger age group of Dr. Vories, so that the two sets of observations are consistent. Our observations are based on intracutaneous tests.

DR. ROSENHOLTZ, St. Paul: I was interested in Dr. Vories' statement that negative Pirquet tests were followed by positive Mantoux reactions. Recently, I saw a child who had been sick for four months. The abdomen had been swollen since the child was 6 months of age. It was 14 months old when I saw it. The Pirquet test had been made. The Mantoux tests with 0.01 mg. and 0.10 mg. were negative. Fluid withdrawn from the abdomen and injected into a guinea-pig produced tuberculosis. At the end of six months, another Pirquet test was done. The patient was given treatment with the ultraviolet lamp. The weight increased, and the abdomen was reduced in size. The Mantoux test was repeated with 0.01 mg., 0.10 mg. and 1 mg. All were negative. The child had not had measles, nor was it cachetic. There was no question of diagnosis, and the Mantoux test even with 1.0 mg., was negative.

A Case of Thymoma. Dr. W. J. Siemsen.

Little was known regarding the family history of an adopted boy, aged 3½ years. He always became blue on crying. In May, 1927, after becoming chilled, he developed a dry cough. Later, he wheezed, and the mother said that there was a rattle in the left lower lung. Labored breathing developed. In June, a diagnosis of thymic enlargement was made. Four treatments with the roentgen ray were given. Twelve hours after the first treatment, there was improvement, which lasted about three days. Little improvement was noted after the other treatments. Later, when he went to bed his lungs seemed to fill and he had choking spells and was unable to expectorate much.



Infiltration of lung.

There is some evidence of infiltration of the lung, as shown in the accompanying illustration. With the sign of developing obstruction present in the child, it would seem that he has a tumor of the thymus rather than an enlarged thymus which had not been greatly influenced by therapy.

[The patient died shortly after this report was made. At necropsy a thymoma was found.]

Flatfoot in Children. Dr. V. B. Dowler.

Varying degrees of flatfoot in 1,574 children from rural schools of from 5 to 15 years of age were analyzed. Examination was made by photograph, footprints and clinical inspection. The results of the last two agreed most satisfactorily. The feet were graded 0, 1, 2, 3 and 4, according to the degree of flatness. A greater proportion of more severe grades of flatfoot was found in the older children. The condition was more pronounced and appeared earlier in girls than in boys. In girls alone did poor posture, sore throat, undernutrition and overnutrition appear to have any relation to the flatfoot.

DISCUSSION

DR. NEFF, Kansas City: I am glad to know that a study of this kind has been made. I should be interested in hearing about other factors in the examination, particularly the variety of symptoms.

DR. E. S. PLATOU, Minneapolis: I should like to know if there is a relation between the incidence of flatfoot in older children and preventive measures and proper care in early childhood.

DR. W. R. SHANNON, St. Paul: I should like to know whether Dr. Dowler believes that flatfoot occurs in early childhood. How correct are these records? How much can one depend on them and should one worry about flatfoot in early childhood, that is, under the age of 2 years?

DR. DOWLER: I cannot make a statement about the relation of flatfoot to symptoms because that was not considered. Few complaints were registered. The question of early care was not gone into in detail, because an attempt was being made to establish standards according to the methods described. The only answer I can make to the question about the reliability of the standard used is that the standard shows that the weight bearing is not on the inside of the foot. If the footprint of the child conformed to the standard, whether or not that is considered correct, it was classed accordingly.

DR. HELMHOLZ: It has been planned to follow a group of children from the second year to see what happens to their feet. That is a part of the study that Dr. Dowler has undertaken.

THREE CASES OF NEPHROSIS. DR. S. AMBERG.

A boy, aged 6 years, had suffered from a severe cold in December, 1925, followed about a month later by puffiness of the eyes, fever, pus, albumin and casts in the urine, and still later by generalized edema. In April, 1926, nine quarts (8,515 cc.) of fluid was removed from the abdomen. The urinary output increased but shortly dropped to 2½ ounces (74.2 cc.) daily. Abdominal paracentesis was done immediately after arrival at the clinic on April 20. Edema of the face and abdomen increased, and a second parencentesis became necessary. The fluid of the first paracentesis was clear, but the second fluid was somewhat cloudy; at a third paracentesis, which became necessary later, the fluid was typical of nephrotic ascites.

In the hospital the boy developed several complications—hydrothorax with severe bronchitis and interlobar pleurisy, a gum boil, a skin lesion and acute appendicitis, for which he was operated on following the acute attack. The tonsils were removed but not because of particular evidence of infection. At that time the sinuses were investigated and the antrum opened but nothing was found. The systolic blood pressure was 130, diastolic, 90. Later it became lower, and sometimes reached the low levels observed in such cases. The albumin content of the serum was low. At first the blood urea was 55 mg. for each hundred cubic centimeters, but it decreased to 17 mg.

Benefit did not result from the administration of thyroid. Ammonium salts with merbaphen were tried. The urinary output increased somewhat, although it remained within normal limits, on the administration of ammonium salts. After abdominal paracentesis and during administration of 4 Gm. of ammonium nitrate daily, the urinary output increased to a maximum of 2,000 cc., but gradually dwindled to about 500 cc. Prolonged seepage after paracentesis helps diuresis. The boy left the hospital in August, and after being home about two weeks he had a sudden dilatation of the heart which was nearly fatal. He returned to the hospital with all symptoms aggravated. At this time the child did not respond properly to administration of ammonium salts and merbaphen. The only thing which helped was paracentesis; shortly after this was done, he was sent to his home, where he died a few months later, apparently in an attack of syncope.

The second case was that of a girl, aged 9 years, who had become ill in the spring of 1926. Puffiness of the legs and eyes had been noted after scarlet fever immunization. She had improved after being placed in bed on a salt free diet. Since a roentgenogram of the sinuses had revealed involvement, they had been opened. The edema had disappeared and she had remained well until August, when she had had a slight cold. The sinuses had been opened a second time. She had been forced to stop school and go to bed. The sinuses had been opened in November and December.

The child came to the clinic in January, 1927, at which time the urine was loaded with albumin, a few red blood cells and few lipoid bodies. Examinations of the nose and throat gave negative results. The child was edematous. The protein content of the serum was 4.3 mg. The lipoids were 783 mg. per cent. The systolic blood pressure was 110, diastolic 88. She was given urea in spite of the fact that the blood urea was 90 mg. The urinary output increased to 800 cc., and the urea content of the blood increased. The child improved until she developed a temperature with signs of peritonitis to which she succumbed four days later. At necropsy, the pathologists diagnosed pneumococcus peritonitis with pronounced involvement of the renal tubules.

The third case was that of a boy, aged 4 years. Five months before admittance to the clinic, he had had a cold and sore throat followed by acute abdominal pain and edema. He had been hospitalized, and apparently an abscess had developed in the right loin from which about 500 cc. of thick pus was removed. He had been well for about six weeks. Then he had had a slight cold followed by marked edema of the face.

On admittance to the hospital, we tried administration of theocin, sodium nitrate and urea. He did well on the urea. At first he was given 5 grains (0.32 Gm.) three times a day, in spite of the fact that the blood urea was 58 mg. There was an increase in cholesterol and a decrease in protein in the blood. The blood pressure was approximately normal but sometimes dropped considerably. The McClure test was normal. The urea decreased to 14 mg. The tonsils were removed because of evidence of infection. The temperature rose to 105 F., and both ears opened. The left mastoid had to be opened and drained. During this time, the child was kept on urea medication, and a return of the edema was not noted. The patient gained in weight and was dismissed improved.

In these cases the blood pressure, the blood urea and sometimes the output of phenolsulphonphthalein varied noticeably. These cases may not be examples of pure nephrosis or, if so, it seems clear that in cases of nephrosis there need not be a rigid set of symptoms.

The naphthol yellow S penetration of nephrotic blood serum into gelatin was demonstrated.

DISCUSSION

Dr. Andrews, Mankato, Minn.: I should like to ask whether these patients showed any reactions from merbaphen in the way of bloody stools, etc. I had one such reaction, and I wondered if you had had any here.

Dr. Amberg: We have not. We have given merbaphen carefully, starting with 0.2 cc., and gradually increasing the amount as necessary. Bloody diarrhea has occasionally been seen in the course of the disease but independent of any medication.

Pathologic Anatomy of Acrodynia. Dr. R. L. J. Kennedy and Dr. J. W. Kernohan.

A report of the pathologic changes in acrodynia including the literature on the subject will be published in detail later.

DISCUSSION

DR. JEANS: I should like to ask whether an anatomic examination of the ears showed any pathologic lesions.

DR. R. TAYLOR, Minneapolis: I should also like to ask about the nasopharynx.

DR. KERNOHAN: The middle and inner ears were examined and no pathologic process was found in them. The nasopharynx was not examined.

FACTORS IN THE DECAY OF TEETH. DR. L. O. KAPPES.

The relation of diet, health and prenatal factors to the condition of the teeth was studied in two groups of school children, one with exceptionally good teeth and one with exceptionally poor teeth.

After the first year of age, vegetables, fruit, meat and eggs predominated in the diet of thirteen of the twenty-five children with good teeth and in only three of the twenty-five with poor teeth, whereas carbohydrates predominated in three of those with good teeth and in fourteen of those with poor teeth.

The various diseases reported occurred eighty-two times in the group with good teeth and 104 times in the group with poor teeth. The average age of the children in the first group was 3.4 years greater than the average age in the second group.

Vegetables, fruit and milk predominated in the diet of the mother during pregnancy in fourteen of the group with good teeth and in ten of those with poor teeth. Carbohydrates predominated in the mother's diet in six of those with good teeth and in ten of those with poor teeth.

In two children with good teeth, poor teeth were found in both parents, and the same condition was found in the parents of eleven of those with poor teeth. Good teeth in both parents were found in seven of the group with good teeth and in none of those with poor teeth.

This paper will be published in full in a future issue.

DISCUSSION

DR. E. D. ANDERSON, Minneapolis: I cannot see from the figures why the conclusion cannot be drawn that heredity is not an important factor. From my observations, it seems that heredity is a large factor. There are certain indications of heredity in abnormalities of the teeth. In delayed dentition, when it is not due to rickets, one will almost invariably find that one or both parents had faulty dentition. The same applies to early dentition. We have all had the experience that children brought up under the best hygienic and dietary conditions will have poor teeth and that one or both parents will have poor teeth. My feeling is that if heredity is not the biggest factor, it is one of the biggest factors.

DR. JEANS: I feel hesitant about making this statement, but I wonder if the same observations under heredity could not be classified under familial traits or under food habits of the family. I wonder if it is possible to separate these two factors.

DR. R. B. BOYD, Iowa City: We have made some observations in our clinic that are relevant to this subject. Every child that comes to the clinic has a careful dental examination. Many return so that we can keep on with the observations. The dentist came to me and asked if I could explain the unusual manifestations in the teeth of diabetic children. He said that in every instance the diabetic children who had been under treatment had evidence of previous dental caries, which was extensive in some cases, but that after treatment for some time the caries was completely arrested; the teeth seemed hard and when examined later did not show evidence of new caries. The dentist had also noted more calcareous deposits on the teeth of diabetic children than on the teeth of others. The group of about forty children examined

includes patients of all types. The same manifestations have not been noted in any other group. There is no possible cause that can be correlated with the symptoms. One pertinent thing is that these children are on a diet high in mineral content and low in carbohydrate. Every child had been on insulin treatment. Care cannot be a marked factor in the arrested dental caries of this group, for some of the patients did not take any care of the teeth whatever.

DR. HELMHOLZ: I must confess that I had more definite ideas as to what caused dental caries than I have now. It is interesting to have Dr. Boyd's report on the diabetic children from which it is evident that the children who received large amounts of carbohydrate and candy are the ones who seemed to have dental caries. My ideas agreed with those of Dr. Anderson, but I have gone over these figures and I do not believe that unless one is a real statistician he could prove that heredity had much to do with dental caries.

DR. KAPPES: The heredity factor as such was not definite in these cases. It is probably true that the dietary factor played a large part in the incidence of good teeth in a family. In talking with the parents and children, I felt that it was difficult to distinguish between the hereditary and dietary factors.

REPORT OF A CASE OF ACUTE CHOREA. DR. H. M. KEPLER.

A girl, aged 11 years, was brought to the hospital because of persistent fever, purposeless motion and delirium. She had been well until an attack of tonsillitis one month before admission. She had apparently recovered, but the condition of the throat had soon reappeared, accompanied by severe pains, redness and swelling of the joints. The temperature had risen to 104 F., and she had become delirious. A few days later, purposeless twitching of the facial muscles had been noted. The symptoms in the joints had subsided several days before admission. A sister of about the same age had developed an infection of the throat, acute polyarthritis, endocarditis, with high fever, delirium and motor irritability which had persisted until death. Necropsy was not obtained in this case.

The child was acutely ill, irrational, and exhibited choreiform grimaces and constant purposeless movements of the trunk and extremities. The tonsils were enlarged and infected. Cervical adenitis was present. There was evidence of mitral endocarditis. Jaundice was not present, and the liver was not palpable. The child had moderate secondary anemia with a high polymorphonuclear leukocytosis. The spinal fluid was sterile and microscopically normal. The Nonne test was positive, but the sugar content normal. A roentgenogram of the chest and an electrocardiogram showed nothing of significance. Culture of the blood was negative at the end of forty-eight hours, but later a feeble growth of green streptococci appeared which produced valvular endocarditis when injected into rabbits.

During the four days in the hospital, the child's mental state varied from muttering stupor to screaming maniacal delirium terminating in coma. Sedatives were ineffectual. The temperature ranged from 101 to 106. Micturition was involuntary from the first, and defecation was involuntary after the third day in the hospital. On this day emesis of a material resembling coffee grounds began and persisted in spite of lavage. The child died on the fourth day. The clinical diagnosis was acute encephalitis with chorea and rheumatic endocarditis.

At necropsy significant pathologic changes were found only in the liver, heart and stomach. The brain was normal. The stomach showed multiple mucosal erosions and contained considerable old blood. There were numerous fine vegetations over the entire peripheral surface of the mitral and aortic valves. The surface of the liver was yellow and mottled. Section showed yellowish areas suggestive of fatty change. This was confirmed by microscopic examination from which a diagnosis of acute yellow atrophy of the liver was made.

Mode of Infection in Pyelitis. Dr. H. F. Helmholz.

Little definite information on the mode of infection in pyelitis has been reported, in spite of all the work that has been done on the subject. From pathologic and clinical studies made at the Mayo Clinic, we have not arrived at any conclusion. A recent report by Chown and one by Schloss state that focal lesions have occurred in the kidney in a large number of cases. Evidence has not been presented as to the mode of infection.

We have been interested in producing renal lesions in rabbits by both intravenous and intracystic injections of colon bacilli in order to compare these with the lesions in children. It happened that a number of cases of bacilluria in rabbits were discovered, and we studied the involvement of the urinary tract in twenty-five such cases by the following technic: If a catheterized specimen of urine revealed organisms, a second catheterization was done to be sure that the organism had actually come from the bladder. The animal was later etherized and both ureters tied. Several hours after coming out from the anesthetic, it was killed by injection of air into one of the veins of the ear. Urine was obtained from the bladder and both renal pelves. In practically all cases, only the urine from the bladder contained bacteria, a fact which would tend to show that the infection traveled by the ascending route rather than by way of the blood stream. In a single instance, the urine from the renal pelvis also showed organisms, and in two other cases bacteria and pus were present in the urine taken from the renal pelvis. These experiments indicate that bacilluria limited to the bladder is common and is the exception in the upper urinary tract. Thus, involvement of the bladder seems to be primary and infection of the upper urinary passages is brought about by ascending infection from the bladder.

DISCUSSION

Dr. Taylor, Minneapolis: What was the sex of the rabbit?

Dr. Helmholz: The pyelitis happened to be in females. About half of the rabbits were males and half females.

Dr. Platou: Was there evidence of infection in other parts of the body?

Dr. Helmholz: None. Many animals have infections of the upper respiratory tract.

Eosinophilia — A Case Report. Dr. R. A. Stephenson.

A girl, aged 19 months, was brought to the clinic in September, 1926. She had been well until two months before, when she developed bronchial pneumonia followed by whooping cough. She had been seriously ill but had made a good recovery. A month previously, the abdomen had become large.

Examination showed a fairly well developed child, who was flaccid and listless. The temperature was 101 F. The abdomen was prominent, with enlarged veins and moderate enlargement in the upper quadrant. The liver and spleen were enlarged. The blood count showed a leukocytosis of 45,000, with 55 per cent eosinophils.

The course in the hospital was marked by complications — an eruption resembling German measles and acute otitis media on the right; the abscess opened spontaneously, shortly after which the glands enlarged and had to be drained. The blood count was uninfluenced by treatment and was practically the same when the patient was dismissed as when she was admitted to the hospital.

I have been unable to find anything in the literature which would correspond to this case. Bass reported a case of eosinophilia in a child, aged 6 years, who had sinusitis and acute infection of the upper respiratory tract. In other reports of cases, the condition occurred in adults and was usually associated with some chronic infection, such as heart disease or leukemia.

DISCUSSION

DR. JEANS: Was fever present?

DR. STEPHENSON: The temperature during the stay in the hospital averaged 102 and 103 F. During the acute complications, it rose to 104.

DR. AMBERG: If I am not mistaken, we made cultures from the pus and injected them into rabbits without finding a change in the blood picture.

DR. TAYLOR: Was this a persistent anemia in which the red blood cells numbered 3,500,000?

DR. STEPHENSON: Yes. The red blood cells numbered 3,520,000 and the hemoglobin content was 41 per cent. There was no evidence of blood destruction. More than 2 per cent of reticulated cells usually were present.

PEDIATRIC SECTION OF THE ACADEMY OF MEDICINE OF CLEVELAND

Seventh Quarterly Meeting, Nov. 30, 1927

H. J. GERSTENBERGER, M.D., *in the Chair*

THE "ACUTE ABDOMEN" OF THE CHILD. DR. JOSEPH BRENNEMANN.

Abdominal conditions in children are always particularly interesting to me, not only because they are serious but because they usually require prompt decisions; "medical bellies" are far more common than "surgical bellies," and for this reason the physician has some advantage over the surgeon in the diagnosis of these conditions. In every acute abdominal condition, two things stand out as most to be feared: "Have we an obstruction?" "Have we an appendicitis?" (or peritonitis?).

Congenital atresia of the esophagus is probably not so rare as is generally believed. I, myself, have seen eight or nine cases. The symptomatology is simple. When the child takes fluids it can take one swallow, possibly two, but after that the fluid comes back through the nose and from the mouth, the child turns blue, then black, chokes, and acts as if it were dying. Before this, however, the condition can often be diagnosed from the fact that there is a constant accumulation of frothy mucus in the nose and mouth. In nearly all of these cases the upper end of the esophagus ends blindly as a dilated sac, and the lower end passes from the stomach as a thinner tube directly into the bifurcation of the trachea. Operative intervention has so far been of no avail and probably never will be.

The vomiting pyloric stenosis nearly always begins in the second or third week after birth. Vomiting immediately after birth is almost never due to pyloric stenosis, nor is that beginning two months after birth. In the early forms, the patients nearly always get well on any rational feeding given frequently enough. In those in whom the feeding is begun after a month or two, the condition yields almost without exception to thick cereal and atropine. In neither type of case is an operation necessary. If the vomitus contains bile, one can be sure that a pyloric obstruction is not present but that in all probability there is a duodenal obstruction just beyond the ampulla.

One has to forget much of one's textbook teaching in order to diagnose an intussusception early, for it usually does not present the classic picture. The patient is generally quiet, appears fairly comfortable, only occasionally cries out, and winces or squirms with each new little pain, but there is not the stormy course that one is led to believe. Most of the infants with intussusception develop a psychic reaction to their environment that is diagnostic; hence,

it is almost possible to recognize an intussusception from the facial expression and actions of the child. The tumor can nearly always be felt, and blood is nearly always present in the stools intimately intermixed. A valuable sign that is almost never absent is the currant "jelly-like" substance that follows the retreating finger after rectal examination. Obstruction due to Meckel's diverticulum is much less frequent and can commonly be diagnosed from the location on the right side and the absence of a sausage-like tumor and of blood in the stools. It is commonly a serious condition. A Meckel's diverticulum is probably the most frequent cause of certain severe painless hemorrhages from the bowels as reported by Abt and Strauss. I have seen about four of these patients.

Another interesting condition is a congenital atresia of the rectum just above the sphincter ani. Most of these patients develop a megacolon and present a markedly distended tympanitic abdomen. The obstruction is commonly so tight that the tip of the little finger cannot be inserted at first. I have recently reported six of these cases in which there was prompt and permanent relief from simple digital dilatation. I am inclined to believe that this condition is probably the etiologic factor in many of the cases that have been diagnosed as Hirschsprung's disease.

In appendicitis in children, the pain usually begins at the umbilicus and then passes to the right lower quadrant of the abdomen. The tenderness, which is of far more diagnostic value, is always in the lower quadrant. Differentiation from the referred pain of pneumonia is usually easy, but if the physician is in doubt, a roentgenogram commonly solves the question. One child was operated on for appendicitis, in whom it was later found that the pain was referred from a pericarditis. The most important single thing in the differentiation of appendicitis is the abdominal pain that occurs with infections of the throat. This pain may be either a referred pain or pain due probably to mesentery glands. While this pain is much more common than appendicitis itself, it must be emphasized that appendicitis itself is frequently a complication of infection of the upper respiratory tract. Any pain in the abdomen occurring with infection of the upper respiratory tract should lead one to think of appendicitis and to be sure to exclude it. Nine of the last ten patients with appendicitis seen in private practice had complications of unquestioned infection of the upper respiratory tract.

DISCUSSION

DR. CORRIGAN: My last two patients with intussusception were seen early, and the intussusception could be reduced manually through the abdominal wall. Neither of these patients were operated on.

DR. SLOAN: I recently saw an infant, aged 4 weeks, with symptoms of complete obstruction. During sleep, however, it passed a large stool. Later, a mass could be felt. At operation a chylous cyst of the mesentery was found. I should like to emphasize the necessity of early operation in acute abdominal conditions in children and the value of blood transfusions.

DR. KELLY: I should like to point out the value of the surgeon knowing diseases of children if he is to work with them. This has generally been neglected. The surgical treatment of children's diseases should be a specialty as well as the medical treatment. As to pyloric stenosis, I believe one will find that fewer and fewer of these patients will require operative treatment. Concerning intussusception, I think there are acute, subacute and chronic forms of this condition. Some last five or six weeks. I have seen several cases in which the intussusception was apparently the result of a fright or a fall.

Intussusception can often be reduced by air or water pressure, but the pressure should always be measured.

Megacolon is not a common condition in my experience. If an operation is performed, it should be done in two or three stages.

DR. EPSTEIN: I have seen one patient in whom the mesenteric glands suppurated. How frequently has Dr. Brennemann seen this condition?

Is the time relation between the pain and the vomiting in appendicitis of any significance?

Is there such a thing as chronic intussusception in which the patient may have pain one day and be free from it the next?

DR. LENHART: Have the cases of obstruction of the urinary tract observed by Dr. Brennemann ever been the result of a mild degree of obstruction? I observed one in which it was due to phimosis.

I once operated on an infant whose condition had been diagnosed as pyloric stenosis. Only slight thickening of the pylorus was found. The symptoms recurred in four or five days, and I was asked to operate again. This time the usual thickened pylorus was found. This emphasizes the fact, I believe, that pyloric stenosis is a progressive condition.

DR. FARGO: I should like to ask Dr. Brennemann to tell us something of the etiology and diagnosis of subphrenic abscess.

DR. GIBSON: I recently operated in two interesting cases of obstruction. The first was a congenital anomaly, a reversed rotation of the mesentery of the jejunum. The second was a volvulus of the upper jejunum caused by a large mass of mesenteric glands. Both the patients died.

DR. BURHANS: What treatment does Dr. Brennemann recommend when he feels that the patient has a pneumococcic peritonitis?

DR. GERSTENBERGER: I must admit that I have not once felt certain that I could palpate the tumor in pyloric stenosis except, of course, when the stomach was in a state of active contraction. I should like to know what procedure Dr. Brennemann follows in trying to palpate the enlarged pylorus.

I wonder whether the experience that Dr. Brennemann has had with atropine is not due to the fact that all of the children so treated seemed to have been given approximately the same dose. I have found that the tolerance of infants for atropine varies a great deal. I have seen some infants present a severe pharmacologic reaction with one drop of a 1:1,000 solution and one infant did not show any reaction with 40 drops of a 1:1,000 solution given five times in twenty-four hours.

DR. BRENNEMANN: In reply to Dr. Corrigan, I would say that I have always thought that probably more of these conditions could be reduced without operation than has been suspected, especially if the patients are seen early; if seen later, I am inclined to think that an operation should be done promptly because of the harm that comes from the trauma of manipulation.

In response to Dr. Epstein's question, I think I have seen two patients in whom a mesenteric gland suppurated — once with a resulting peritonitis and once with rupture into the rectum. In my experience, I am not familiar with any importance attaching to the time relation between the pain and vomiting in appendicitis. There is said to be such a thing as chronic intussusception. I have never seen one last more than ten days. In the intussusceptions that last longer, I am inclined to think that usually the condition is a recurrent affair instead of a chronic intussusception. I saw one such case last for a long time in which there was a prolapse of the intussusception. This case was recently reported by Dr. Kato and Dr. Markey.

The observation that Dr. Lenhart records with reference to the nature of pylorus at two different periods is one of the most interesting things that I have heard. If he has careful notes on this case, I think that it should be published, because it is just such information, and such information only, that can ultimately tell why pyloric stenosis acts as it does and how much of it is due to hypertrophy and how much to simple spasm. In the patients with obstruction of the urinary tract that I have seen, there has nearly always been a severe degree of obstruction. I have never seen one due to phimosis.

I am afraid I have nothing of interest to tell Dr. Fargo concerning the etiology and diagnosis of subphrenic abscess.

The treatment of pneumococcic peritonitis is, at best, unsatisfactory. If the course is at all stormy or operation is performed early, nearly all of the patients die. Dr. Burhans perhaps will remember a report from the Baby's Hospital of New York (I think it was Bartlett and Wollstein's report), in which the physicians reached the conclusion that almost the only patients who lived were those in whom the condition was allowed to go on to localization of the abscess with subsequent drainage. There is always a serious question as to what ought to be done when one is confronted by pneumococcic peritonitis.

I agree with Dr. Gerstenberger that the pyloric tumor is often hard to find. In an emaciated infant with a definite tumor, it is not so hard to palpate. I think the best time to feel for the pylorus is just after a little food or water has been taken or immediately after a vomiting spell. Infants do seem to vary a great deal as to their tolerances to atropine, but it is also perhaps worth recording that atropine varies a great deal, depending on how old the solution is.

One further interesting abdominal condition that may simulate appendicitis is ovarian tumor with a twisted pedicle. I have seen several of these, and the patients nearly all have an enormously high leukocyte count which is of diagnostic value. One patient had 90,000 leukocytes; another more than 40,000.

Book Reviews

DIAGNOSTIK UND THERAPIE DER KINDERKRANKHEITEN. By F. LUST, M.D. Price, 10.50 marks. Pp. 523. Berlin: Urban & Schwarzenberg, 1927.

The author calls the book a guide for the practicing physician, and it is not intended for the pediatrician. It gives only concise summaries, which are good in most instances and lays great stress on treatment, the outlines of which are, in general, satisfactory. The chapters on nephritis could be improved by revision. It is somewhat peculiar to read about the "lubricating action" of a drug in constipation. This phrase, although much used, has little meaning. The amounts of methenamine which are recommended for use in pyelitis are insufficient. The definition of acrodynia is given as "the vegetative neurosis (Akrodynie, Feersche Krankheit)." To call this disease a neurosis of the vegetative nervous system is not an advancement.

A chapter is devoted to therapeutic technic; the second part of the book deals with the drugs given to children and contains directions for the feeding formulas most commonly used abroad. This second part also has a list of sanitariums for children. On the whole, relatively few objections can be raised to the text.

POTASSIUM AND TARTRATES. By RALPH W. WEBSTER, PH.D., M.D. Price, $2.50. Pp. 168. Chicago: The Commonwealth Press, 1927.

This book contains a nice summary of the literature on potassium and tartrates. On the paper cover is found the note, "This book is published at a time when new facts are being presented against the use in foods and drugs of cream of tartar, tartrates in general, and potassium salts." This explains the peculiar combination of subjects covered in the book.

Directory of Pediatric Societies

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SECTION OF DISEASES OF CHILDREN

Chairman: Dr. Hugh McCulloch, 500 S. Kingshighway, St. Louis.
Secretary: Dr. C. A. Aldrich, 545 Lincoln Ave., Winnetka, Ill.
Place: Minneapolis. Time: June 11-15, 1928.

AMERICAN PEDIATRIC SOCIETY

President: Dr. J. Claxton Gittings, 1828 Pine St., Philadelphia.
Secretary: Dr. Howard Childs Carpenter, 1805 Spruce St., Philadelphia.
Place: Washington, D. C. Time: April 30 to May 2, 1928.

THE ASSOCIATION OF AMERICAN TEACHERS OF THE DISEASES OF CHILDREN

President: Dr. J. P. Crozier Griffith, 1810 Spruce St., Philadelphia.
Secretary: Dr. Paul W. Emerson, 86 Bay State Road, Boston.
Place: Minneapolis. Time: June 12, 1928.

AMERICAN CHILD HEALTH ASSOCIATION

President: Hon. Herbert Hoover, 370 Seventh Ave., New York.
Secretary: Dr. Philip Van Ingen, 370 Seventh Ave., New York.
Place: Undecided. Time: May or June, 1928.

CANADIAN SOCIETY FOR THE STUDY OF DISEASES OF CHILDREN

President: Dr. G. R. Pirie, 20 Madison Ave., Toronto.
Secretary: Dr. A. P. Hart, 1844 Bloor St. West, Toronto.
Place: Vancouver, B. C. Time: June, 1928.

SECTIONAL

CENTRAL STATES PEDIATRIC SOCIETY

President: Dr. H. T. Price, 121 University Place, Pittsburgh.
Secretary: Dr. A. H. Parmelee, 310 S. Michigan Ave., Chicago.

SECTION ON PEDIATRICS OF SOUTHERN MEDICAL ASSOCIATION

President: Dr. Robert A. Strong, Pass Christian, Miss.
Secretary: Dr. Hugh L. Dwyer, Medical Arts Bldg., Kansas City, Mo.

LOCAL

NORTHERN CALIFORNIA PEDIATRIC SOCIETY

President: Dr. W. L. Channell, Medical Bldg., Oakland, Calif.
Secretary: J. E. Parrott, Medico-Dental Bldg., San Francisco.
Place: Various Teaching Schools. Time: Monthly.

SOUTHWESTERN PEDIATRIC SOCIETY

President: Dr. Oscar Reiss, Westlake Professional Bldg., Los Angeles.
Secretary: Dr. William Sidney Bowers, 1136 West 6th St., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

THE ROCKY MOUNTAIN PEDIATRIC SOCIETY

President: Dr. W. Wiley Jones, Majestic Bldg., Denver.
Secretary: Dr. Berryman Green, 537 Republic Bldg., Denver.
Place: Children's Hospital, Denver. Time: Third Saturday of each month, 2:30 p. m., September to May, inclusive.

GEORGIA PEDIATRIC SOCIETY

President: Dr. Joseph Yampolsky, 127 Peachtree St., Atlanta.
Secretary: Nevin M. Atkins, Atlanta.
Place: Savannah, Ga. Time: May 9, 1928.

PEDIATRIC SECTION OF FULTON COUNTY MEDICAL SOCIETY, ATLANTA, GA.

President: Dr. William W. Anderson, 362 Peachtree St., Atlanta.
Secretary: Dr. Lee Bivings, Exchange Bldg., Atlanta.
Place: Academy of Medicine, 32 Howard St., Atlanta.
Time: Second Thursday of each month from October to April, at 8 p. m.

NEW ENGLAND PEDIATRIC SOCIETY

President: Dr. James Herbert Young, 66 Commonwealth Ave., Boston.
Secretary: Dr. Thomas Lanman, 286 Marlborough St., Boston.
Place: Boston Medical Library. Time: Second Friday of each month.

CHICAGO PEDIATRIC SOCIETY

President: Dr. Maurice Blatt, 30 N. Michigan Ave., Chicago.
Secretary: Dr. J. K. Calvin, 104 S. Michigan Ave., Chicago.
Place: City Club. Time: Third Tuesday of each month.

LOUISIANA STATE PEDIATRIC SOCIETY

President: Dr. L. R. De Buys, 1487 Delachaise St., New Orleans.
Secretary: Dr. F. J. Kinberger, 3601 Prytania St., New Orleans.

DETROIT PEDIATRIC SOCIETY

President: Dr. George E. White, Capitol Theatre Bldg., Windsor, Ontario, Canada.
Secretary: Dr. W. S. O'Donnell, 1563 David Whitney Bldg., Detroit.
Place: Children's Hospital of Michigan. Time: No fixed date; approximately once a month.

NORTHWESTERN PEDIATRIC SOCIETY

President: Dr. F. W. Schlutz, University of Minnesota, Minneapolis.
Secretary: Dr. E. S. Platou, 730 La Salle Bldg., Minneapolis.
Place: University Campus and Rochester. Time: Winter, Spring, Summer, Fall.

ST. LOUIS PEDIATRIC SOCIETY

President: Dr. T. Wistor White, Lister Bldg., St. Louis.
Secretary: Dr. E. H. Rohlfing, 816 Beaumont Medical Bldg., St. Louis.
Place: St. Louis Children's Hospital. Time: At least once a year and contingent thereafter on the arrangement of a suitable program.

NEBRASKA-IOWA PEDIATRIC SOCIETY

President: Dr. Floyd Clarke, 731 City Nat'l Bank Bldg., Omaha.
Secretary: Dr. R. B. Eldredge, 1036 Medical Arts Bldg., Omaha.
Place: Add-Sell Restaurant. Time: Second Thursday of each month from October to May, inclusive, 6 p. m.

BROOKLYN PEDIATRIC SOCIETY

President: Dr. Louis M. Ruderman, 961 Eastern Parkway, Brooklyn.
Secretary: Dr. Joseph F. Paulonis, 1357 Bushwick Ave., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Last Wednesday of each month, except June, July and August.

BRONX PEDIATRIC SOCIETY

President: Dr. William Hinz, 1964 Grand Concourse, New York.
Secretary: L. H. Barenberg, 1749 Grand Concourse, New York.
Place: Concourse Plaza, 161st, St., and Grand Concourse, New York. Time: Second Wednesday of each month, except June, July, August and September.

CENTRAL NEW YORK PEDIATRIC CLUB

President: Dr. Frank Vander Bogert, 111 Union St., Schenectady, N. Y.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany, N. Y.
Place: Various Cities in New York. Time: Fourth Thursday of October, January and April.

PEDIATRIC SECTION OF THE NEW YORK ACADEMY OF MEDICINE

President: Dr. William Ropes May, 8 East 66th St., New York.
Secretary: Dr. Stafford McLean, 17 East 71st St., New York.
Place: New York Academy of Medicine, 2 East 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

THE PEDIATRIC SECTION OF THE ACADEMY OF MEDICINE OF CLEVELAND

Chairman: Dr. J. W. Epstein, 3912 Prospect Ave., Cleveland.
Secretary: Dr. Charles W. Burhans, 14805 Detroit Ave., Lakewood, O.
Place: 2009 Adelbert Road. Time: Four meetings, from September to May.

PEDIATRIC SECTION, ACADEMY OF MEDICINE, TORONTO

President: Dr. M. A. Cox, 34 St. Clair Ave. West, Toronto.
Secretary: Dr. F. R. Hassard, 1361 King St. West, Toronto.
Time: November 17, December 15, February 16 and March 15.

PHILADELPHIA PEDIATRIC SOCIETY

President: Dr. Edward L. Bauer, Jefferson Medical College, Philadelphia.
Secretary: Dr. John Porter Scott, 2040 Pine St., Philadelphia.
Place: College of Physicians, 19 S. 22nd St., Philadelphia. Time: Second Tuesday of each month from October to June, inclusive.

MEMPHIS PEDIATRIC SOCIETY

President: Dr. W. D. Blue, 1024 Madison Ave., Memphis, Tenn.
Secretary: Dr. Gilbert J. Levy, 899 Madison Ave., Memphis, Tenn.
Place: Memphis General Hospital. Time: Second Tuesday of each month.

TEXAS PEDIATRIC SOCIETY

President: Dr. Lucius D. Hill, Medical Arts Bldg., San Antonio.
Secretary and Treasurer: Dr. Edwin G. Schwarz, Medical Arts Bldg., Fort Worth.
Place: Galveston. Time: May 9, 1928.

RICHMOND PEDIATRIC SOCIETY

President: Dr. Howard Urbach, 1331 Grove Ave., Richmond, Va.
Secretary: Dr. W. Ambrose McGee, West End Medical Bldg., 2618 Grove Ave., Richmond, Va.
Place: Westmoreland Club, 601 E. Grace St., Richmond, Va.
Time: First Thursday of each month (other than during the summer).

VIRGINIA PEDIATRIC SOCIETY

President: Dr. Lawrence T. Royster, University, Va.
Secretary: Dr. William B. McIlwaine, Petersburg, Pa.
Place: Danville, Va. Time: October 17, 1928.

NORTH PACIFIC PEDIATRIC SOCIETY

President: Dr. R. S. Miles, Fidelity Bldg., Tacoma, Wash.
Secretary: Dr. D. M. Dayton, 704 St. Helens Ave., Tacoma, Wash.

SEATTLE PEDIATRIC SOCIETY

President: Dr. George B. McCulloch, Cobb Bldg., Seattle.
Secretary: Dr. C. L. Smith, Stimson Bldg., Seattle.
Place: College Club. Time: Third Friday of each month, at 7 p. m.

MILWAUKEE PEDIATRIC SOCIETY

President: Dr. A. B. Schwartz, 418 E. North Ave., Milwaukee.
Secretary: Dr. M. G. Peterman, 167 Seventeenth St., Milwaukee.
Place: Children's Hospital, Milwaukee. Time: Second Wednesday of each alternate month, beginning with February.